This thesis has been digitised as part of a Library project to commemorate Warwick's 50th anniversary. The project closely connects with Warwick 50's key themes of celebrating our international research, individual achievement, connecting alumni and leaving a lasting legacy.

University of Warwick institutional repository: http://go.warwick.ac.uk/wrap

A Thesis Submitted for the Degree of PhD at the University of Warwick

http://go.warwick.ac.uk/wrap/3641/

This thesis is made available online and is protected by original copyright.

Please scroll down to view the document itself.

Please refer to the repository record for this item for information to help you to cite it. Our policy information is available from the repository home page.

Working Memory in N-Back Tasks: ERP Studies

by

Yung-Nien Chen, M.D.

A thesis submitted in partial fulfillment of the requirements for the degree

of Doctor of Philosophy in Psychology

University of Warwick, Department of Psychology

September 2007

Table of Contents

List of Illustrations and Tables

Acknowledgement

I would like to acknowledge my supervisors Dr. Suvobrata Mitra and Dr. Friederike Schlaghecken. Without their guidance, as a neurologist without psychological background, I cannot cross the border of such a complex and mysterious field. In addition, I would like to acknowledge my wife. She sacrificed dentist's career to be a housewife and brought our daughter up in a foreign country. Without her support, I cannot finish my PhD course without distraction.

Summary

Three event-related potential (ERP) experiments investigated the spatial-verbal dichotomy (emphasized by Baddeley's model of working memory), selective attention (emphasized by Cowan's model), and sub-processes in n-back tasks. The studies provide a basis for further clinical research on Alzheimer's disease.

Experiment 1 studied the spatial-verbal dichotomy using n-back tasks with top-down control. It used identical stimuli in both spatial and verbal tasks, and was designed to eliminate interference from perceptual processes. The spatial and verbal tasks differed only in the instructions given before the tasks. Using a model of the task, sub-processes involved in n-back tasks were delineated and analyzed by difference waveforms of ERPs. Domain-specific lateralization was found in a shift sub-process but not in a replacement sub-process. Because information from the irrelevant domain could not be totally excluded by top-down control (which distinguished the spatial and verbal tasks), Experiment 2 recorded information from irrelevant domains. Interactions between irrelevant and relevant domains were found in ERP difference waveforms. Therefore, the results of Experiment 2 suggest that selective attention is unable to exclude interference from the irrelevant domain. Following this conclusion, Experiment 3 adopted a data-driven (bottom-up controlled) methodology, and used different stimuli in spatial and verbal domains in contrast with Experiment 1. In Experiment 3, selective attention was not needed to distinguish spatial tasks from verbal tasks because the spatial and verbal stimuli were different. A different pattern was obtained in Experiment 3; domain-specific lateralization was found only in the replacement sub-process (and not in the shift sub-process). Relationships among n-back task sub-processes, *i.e.*, matching, replacement and shift were determined in advance by logical analyses. From this model, process-specific patterns of domain-specific lateralization, where domain-specific lateralization should exist in the shift sub-process of a conceptual task and in the replacement sub-process of a data-driven task, were predicted under conceptual and data-driven control. The results in Experiment 1 and 3 fitted these predictions, consistent with the proposed logical hypothesis of sub-processes. The similarity between match-specific and domain-specific lateralization suggests avenues for further studies. Using the framework of the model developed here, further investigation could be carried out at the sub-process level using the high temporal resolution of ERPs to decipher the detailed steps of processing that our brains execute in working memory tasks.

Abbreviations

AD	Alzheimer's disease
ANOVA	analysis of variance
DLPFC	dorsolateral prefrontal cortex
EEG	electroencephalogram
ERPs	event-related potentials
fMRI	functional magnetic resonance image
MEG	magnetoencephalogram
MTL	medial temporal lobe
PET	positron emission tomography
PFC	prefrontal cortex
PhD	doctor of philosophy
RT	response time
SSVEP	steady-state visual evoked potentials
TMS	transcranial magnetic stimulus
VLPFC	ventrolateral prefrontal cortex
WM	working memory

Chapter 1. Introduction

1.1. What is referred to as working memory?

The term working memory (WM) has been used within cognitive psychology to refer to the system for temporary maintenance and manipulation of information during a task (Baddeley, 2002).

1.2. WM models

Two viewpoints on information processing are frequently applied: Baddeley's and Cowan's.

1.2.1. Baddeley's model

The first one is a computer-like model: domain-specific storage subsystems controlled by a central processing unit. The multi-component model proposed by Baddeley and Hitch (1974) is the most influential one for WM, consisting of a visuospatial sketchpad for storing and manipulating visual and spatial information, a phonological loop for the corresponding function on phonemic sound information, and a central executive to control attention and supervise both buffers (Baddeley & Hitch, 1994). The visuospatial sketchpad was supported by evidence of selective interference with imagery: the sketchpad can be disrupted by requiring participants to repeatedly process a specified pattern of locations or keys, a procedure that blocks the use of visuospatial imagery (Baddeley & Lieberman, 1980). The phonological loop was evidenced by the effects of phonemic similarity (immediate serial recall of items that

are similar in sound is poorer than that of dissimilar items, Conrad & Hull, 1964), articulatory suppression (with the repetition of an irrelevant sound such as the word 'the', the word length effect disappears, Baddeley et al., 1975), irrelevant speech (articulatory suppression eliminates the effect of phonological similarity when material is presented visually but not auditorily, Baddeley, Lewis, & Vallar, 1984; Murray, 1968), and word length effects (the word length effect stems from the greater fragility of multi-component long words to the processes involved in forgetting, Neath and Nairne,1995, and Brown and Hulme, 1995). Traces within the phonological store were assumed to decay over a period of about two seconds (Baddeley & Hitch, 1974). The question of whether short-term forgetting of the phonological loop represents trace decay or interference remains unresolved (Baddeley, 2002). The central executive is proposed to be an attentional control system which has access to long-term memory and is supported by the two buffer systems mentioned above. One of the functions of the central executive is to integrate information from many different sources (Baddeley, 1986). The central executive is assumed to play a role in many cognitive tasks, including those requiring working memory and was supported by deficits observed in Alzheimer's disease (AD). AD patients may have central executive impairment, resulting in the impairment of task performance that would appear to depend on the central executive (Baddeley, Bressi, Della Sala, Logie,

& Spinnler, 1991). There is a very clear tendency in patients for dual task performance to be impaired while single task performance is maintained. A new fourth system called the "episodic buffer" is also suggested as a supportive buffer for the central executive, which acts as the interface between the sub-systems and long-term memory (Baddeley, 2002). The performance of processing-and-storage tasks is not clearly distinguishable from storage-oriented tasks in the visuospatial domain whereas it is distinguishable in the verbal domain (Miyake, Friedman, Rettinger, Shah, & Hegarty, 2001). This suggests that the visuospatial sketchpad has a closer relationship with the central executive than the phonological loop.

1.2.2. Cowan's model

The second viewpoint is that WM is only a temporary emergence of neuronal activity in the pool (of the whole nervous system). Cowan formulated a model of information processing integrating memory storage, selective attention, effortful versus automatic processing, and interactions between these areas (Cowan, 1988).

Cowan's Embedded-Processes Model is a broad-scope information processing framework originally developed to synthesize a large array of findings on attention and memory. The mnemonic function preserves information that can be used to do the necessary work. In this point of view, the memory storage in Cowan's model is WM per se. Some researchers prefer to define working memory functionally by

stating that any processing mechanism that contributes to the desired outcome is said to participate in the working memory system (e.g., Cowan, 1988). In contrast, some researchers prefer to define working memory according to the mechanisms themselves (e.g., Engle, Kane & Tuholski, 1999). Though Cowan's framework has much in common with those of other researchers, a functional definition of working memory seems more likely to encourage a consideration of diverse relevant mechanisms. Some theories of working memory equate it to focus of attention and awareness (Baddeley, 1993) and some equate it to the sum of activated information (Atkinson and Shiffrin, 1971).

There are two phases of sensory storage in Cowan's model (Cowan, 1988). The first phase extends sensation for several hundred milliseconds, whereas the second phase is a vivid recollection of sensation. A distinctive aspect of the model is that attentional focus is determined by automatic attending (Shiffrin and Schneider, 1977), the automatically preferred processing of cues that have been well-learned, without the need for an attentional filter. In other words, this model emphasizes automatic rather than effortful processing in the first phase. Interference between tasks that occurred in the retrieval of a verbal load during maintenance of a visual array suggested that verbal and visual loads are stored together in the same buffer (Morey & Cowan, 2005). The accuracy of the task that maintained a visual array was reduced

during maintaining verbal loads, especially when these items were read aloud. According to this view, all input information is stored in domain-general neural networks, but they are retrieved and revived only when attention applies. Whether a stimulus is spatial or verbal is not determined by the nature of information while storing the data, but by attention while reviving them. For example, the location of a verbal code would be retrieved if participants were asked about spatial attributes.

1.2.3. Major differences between models

The major differences between these two models are: first, buffers in Baddeley's model are domain-specific whereas the buffer in Cowan's model is domain-general; second, an independent central executive controls both buffers in Baddeley's model whereas the attentional focus in Cowan's model is WM *per se* and refers to only a small part of the so-called buffer. Although different in buffers, both models separate executive functions from storage and suggest that the latter is manipulated by the former.

1.3. Categories of WM

Working memory can be viewed in multiple aspects: by models or by tasks. In both Baddeley and Cowan's models, attentional and executive functions are viewed as an

independent unit. Separate spatial and verbal buffers are suggested in Baddeley's model but a domain-general buffer was suggested in Cowan's model. Because the kinds of buffers are different among models, it is possible that different models have different information processing. Furthermore, different tasks also possibly have different information processing. Because WM is defined as the system for temporary maintenance and manipulation, namely information processing during a task, it is possible that different models and tasks define different kinds of WM.

1.3.1. Spatial-verbal dichotomy

The spatial-verbal dichotomy is emphasized in Baddeley's model. Early lesion studies suggested that the right hemisphere is related to spatial information processing (McFie, Piercy, & Zangwill, 1950) and the left hemisphere is related to verbal information processing (Alekoumbides, 1978). Thus, hemispheric specialization in information processing is *domain-specific*. Given the bilateral distribution of several sensory-specific brain areas, this generalized conclusion cannot be applied to more specific regions. Hemispheric specialization in the PFC is considered as domain-specific between spatial and verbal materials, where verbal materials activated the left prefrontal cortex (PFC) and visuospatial materials activated the right PFC (Awh, Jonides, & Reuter-Lorenz, 1998; Casasanto, 2003; Goldman-Rakic, 2000;

Smith & Jonides, 1999) or *process-specific* between maintenance and manipulation (Owen *et al.*, 1998; Petrides, 1994). In addition to visual materials, an ERP study during auditory N-back tasks (Anourova *et al.*, 1999) showed that there was also a load-dependent segregation between spatial and non-spatial information processing in auditory working memory.

In addition to topographical differences, spatial-verbal differences in the time course of processing were also studied. An ERP experiment requiring participants to maintain memoranda for arithmetical tasks and recording during a task requiring rapid storage, modification and retrieval of multiple stimuli showed that synchronous peaks were distributed in occipital, parietal and prefrontal sites from 130 ms after stimulus onset and continuing after 500 ms (Halgren, Boujon, Clarke, Wang, & Chauvel, 2002). Activity reflecting visual processing occurred in the visual association cortex from 90 to 130 ms, and projected to fronto-parietal areas from 130 to 280 ms, then the activity reflecting visual processing occurred from 300 to 400 ms back to the visual scratchpad in the dorsolateral occipital cortex. Following that, there was a second reversal from 420-600 ms back to frontal-parietal sites for data renewal. Lateralized perisylvian oscillations suggested an articulatory loop. A fronto-centro-parietal 'central executive', an occipital visual scratch pad, a perisylvian articulatory loop and limbic monitor have interactions to complete the sequential stages of a complex

mental operation. This experiment showed interactions among the visual scratch pad, articulatory loops and the central executive.

The spatial-verbal dichotomy is not clear-cut in some respects. A magnetoencephalographic (MEG) study showed that the maintenance of words in working memory activated superior frontal gyri, DLPFC, and superior and inferior parietal lobes, which are traditionally associated with visuospatial working memory (Campo, Maestu, Ortiz *et al.*, 2005). Thus, the words were processed as if they were visuospatial information.

To sum up, the spatial-verbal dichotomy has been studied in topography and time course with different WM tasks, showing left-right hemispheric differences in the frontal lobe and the whole brain, and different time course of activity in the areas associated with spatial or verbal processing.

1.3.2. Storage-executive dichotomy

Both Baddeley and Cowan's models comprise of two different components: information storage and the executive that operates the storage. Cohen *et al.* (1997) has studied this dichotomy with fMRI. N-back tasks were used with time-sustaining memory loads to test active maintenance of memory and time-changing memory loads to test manipulation. Traditional views suggested that manipulation would activate the PFC, whereas active maintenance of information would activate more posterior

regions. Cohen et al.'s study reported that not only posterior regions but also PFC was involved in active maintenance. In addition to this frontal-posterior difference, another fMRI study suggested that evidence of both manipulation and maintenance activity existed in PFC, but DLPFC activity was greater in manipulation (D'Esposito, Postle, Ballard, & Lease, 1999). In contrast to N-back tasks, Sternberg tasks (item-recognition tasks) (Sternberg, 1966) separate retention and recognition, which enables us to investigate maintenance between these two steps. An MEG study using Sternberg tasks with visually presented digits (Jensen & Tesche, 2002) suggested theta oscillations generated in the frontal areas during tasks requiring memory maintenance. An fMRI study during memory tasks with number-letter distracters (Sakai & Passingham, 2004) showed that both PFC and medial temporal lobes (MTL) were involved in memory retrieval. PFC was involved in interference resolution and MTL in rehearsal or reactivating stored information. Transcranial magnetic stimulation (TMS) and lesion studies (Pierrot-Deseilligny, Muri, Nyffeler, & Milea, 2005) showed that the DLPFC controlled short-term spatial working memory, whereas medium-term spatial memory (after 25 s) might be controlled by the MTL. An fMRI study using verbal working memory tasks reported that both maintenance and manipulation were affected in schizophrenia (Tan, Choo, Fones, & Chee, 2005). Left frontoparietal activation increased during the task. In patients, manipulation

was more affected than maintenance, and DLPFC activation was relatively reduced but VLPFC activation relatively increased, in comparison to normal persons. The results suggest that DLPFC is related to manipulation and VLPFC is related to maintenance.

1.3.3. Attentional and executive functions

Although working memory is defined as the temporary buffer in tasks, the majority of WM studies are not related to the stored materials, but to process-specific functions (Kessels, Postma, Wijnalda, & De Haan, 2000). Thus, what they studied was theoretically linked to the central executive in Baddeley's model, whose function is to control attention and supervise both buffers (Baddeley & Hitch, 1994). Attentional control is part of WM (the function of the central executive) in Baddeley's model whereas attentional focus is in actually WM *per se* in Cowan's model. Whether something is in attentional focus is usually indicated by the variation of efficiency in information processing (e.g., response time or accuracy). In addition to direct task performance, researchers also use interference to show the effects of attention. Precisely speaking, attention is regarded as the ability to resolve interference.

1.3.3.1. Dual tasks

An age-comparison study suggested that dual tasks are specific to testing attention and executive functions (Holtzer, Stern, & Rakitin, 2005). In single tasks, memory and motor speed were strongest predictors of age, whereas in dual tasks, the attention and executive factors were the most important predictors of age. The ability to ignore irrelevant information is an important difference between working memory and long-term memory (Oberauer, 2001). Patients with frontal lobe lesions and dys-executive syndrome showed impairment for dual-task coordination, but no impairment in card sorting (a single visuospatial task) and verbal fluency (a single verbal task) (Baddeley, Della Sala, Papagno, & Spinnler, 1997).

Topographical and temporal pattern variations were shown during dual tasks. A functional magnetic resonance image (fMRI) study on dual task performance showed activation of the prefrontal cortex (PFC) when both tasks were performed together, but inactivation when they were performed separately (D'Esposito *et al.*, 1995). Activation gain with increasing task loading was also smaller in patients. Another study demonstrated that thalamic and medial prefrontal cortical regions were activated in a decision-making task for ambiguous categorization, which reflected the function of the central executive (Scott, Holmes, Friston, & Wise, 2000). The more ambiguous difference caused the less activation. In contrast, tasks detecting auditory spatial memory could be performed without prefrontal activation, which suggests no

central executive participation (Kaiser, Walker, Leiberg, & Lutzenberger, 2005).

1.3.3.2. Interference exclusion

The ability of interference exclusion was shown in a Sternberg's task where a cue was given after a memory set to indicate whether the set was relevant or irrelevant. Increasing the set size usually causes longer response time in the Sternberg's task. Setsize effects to negative probes (i.e., probes were from the irrelevant memory set) last for only one second after the cue. In contrast, setsize effects to intrusion probes (i.e., probes that were not from the irrelevant memory set) last for at least five seconds after the cue. These results suggested that irrelevant information is excluded in working memory after one second. Studies on exclusion also suggested that attentional focus has limited capacity and is liable to interference. A study using N-back tasks suggested that only one item could fall within attentional focus at a time (McElree, 2001). The inability to perfectly maintain a target in focus was evidenced by decrease of accuracy. Other information outside attentional focus should be retrieved though a slow *search* process, which was evidenced by the difference in accuracy between inclusion and exclusion tasks. A study on twin pairs showed that memory search rate is heritable (Stins *et al.*, 2005).

Neurophysiological studies have also used interference to study selective attention. An event-related potential (ERP) study using distracters in auditory

memory tasks revealed differences in attention allocation between distracter and memorized items (Wolach & Pratt, 2001). The N1 (about 200 ms) and P2 (about 200 ms) components differed between distracter items and memorized items, indicating different attention allocation. The P2 and N2 (about 300 ms) components indicated differences between probes. P2 was enhanced in response to target stimuli ("go" response), whereas N2 was enhanced in response to non-target stimuli ("no-go" response). The P3 component indicated different speeds of scanning and comparison. P3a amplitude increased with increasing memorized set size, whereas amplitudes in late P3 components (P3b and P3c) increased with faster and more accurate response. Another ERP study revealed that distraction elicited a negativity followed by P3a (350 ms post-stimulus) and then a re-orienting negativity (500 ms post-stimulus) (Berti & Schroeger, 2001). This result suggested that irrelevant information causes an attention shift.

Further studies focused on spatial attention research. Selective attention that shifts on a trial-by-trial basis is called *transient* selective attention (where participants are informed of the target by a precue at the beginning of every trial), whereas selective attention that is focused on the same location during the entire experimental block is called *sustained* selective attention where participants are instructed about the relevant location for an entire block at the beginning of it. P1 and N1 were similar in

both transient and sustained selective attention, but in the transient condition these components had shorter latencies and larger amplitudes than in the sustained condition (Eimer, 1997). P3 target effects in non-spatial visual attributes only appeared in sustained selective attention conditions but not in transient selective attention conditions.

1.3.3.3. Anatomical relationships

Frontal areas were suggested to be involved in attentional and executive functions by neurophysiological studies. Single cell recordings in monkeys reported that the lateral PFC provided top-down control during visual working memory tasks (Kessler & Kiefer, 2005). The PFC counteracted interference, whereas the middle temporal lobe was involved in retrieval. A magnetic resonance spectrometry (MRS) study showed N-acetylaspartate in the dorsolateral PFC (DLPFC) correlated with activation of the working memory network including the DLPFC, temporal and inferior parietal cortices (Bertolino *et al.*, 2000). An fMRI study revealed that anterior PFC was more active during the recognition phase in a working memory task, and more active in response to non-target probes than to target probes (Leung, Gore, & Goldman-Rakic, 2005). These findings support the conclusion that the anterior PFC is involved in working memory, especially in the processes of target and non-target

stimulus distinction. A lesion study of the rat striatum (Bailey & Mair, 2004) reported a double dissociation between visuospatial response time and radial maze, delayed non-matching tasks. Dorsal prefrontal lesions caused attentional impairment that had not been noted in striatal or thalamic lesions and suggested contributions of PFC to attention. The dissociation between lateral PFC activity and basic memory demand suggests that the function of the lateral PFC is to reorganize information and thus reduce task difficulty (Bor, Cumming, Scott, & Owen, 2004). Mathematically structured sequences encourage chunking and elicit greater lateral PFC activation. An fMRI study using N-back tasks with letters and fractal figures showed that maintenance (1-back minus 0-back) activated inferior parietal and DLPFC, with activation in right ventrolateral PFC (VLPFC) in letter tasks and left lingual gyrus in fractal tasks (Ragland *et al.*, 2002). Maintenance plus manipulation (2-back minus 0-back) activated inferior parietal, Broca's area, insula, DLPFC and ventral PFC, with greater right DLPFC activation for letter tasks. Manipulation-only (2-back minus 1-back) produced equivalent DLPFC and anterior cingulated activation in both tasks. Nevertheless, a study on patients with partial frontal lesions suggested that executive processes are not exclusively sustained in the frontal cortex because no difference was seen between normal subjects and patients during dual tasks (Andres & Van der Linden, 2002). An ERP study revealed that the spatial orienting (instruction to

attend to location) is mediated by a left-hemisphere dominant parietal-frontal system, whereas temporal orienting (instruction to attend to time interval) is associated with sensorimotor areas (Nobre, 2001). An fMRI study on multiple sclerosis patients with attention and working memory disorder (Cader, Cifelli, Abu-Omar, Palace, & Matthews, 2006) reported that patients showed relatively reduced activation in the superior frontal and anterior cingulate gyri than normal persons. A magnetoencephalogram (MEG) study showed that early spikes or slow waves indicate attention or task relevance (Aine, Stephen, Christner, Hudson, & Best, 2003). Early spike-like activity (200 ms post-stimulus) was evoked by a visual working memory task. In an auditory task, this spike was absent but replaced by slow waves. These auditory-presented words evoked activity in occipital cortex even though visual stimuli were not present. Prefrontal activity by the working memory task, which was along the superior frontal sulcus, was active later than the earliest effect of attention modulation in visual cortex. This suggests that visual input is auto-focused.

1.3.3.4. Impairment of attentional and executive functions in diseases

Impairment in active processes of working memory was suggested as a feature of early Alzheimer's dementia (Vecchi, Saveriano, & Paciaroni, 1998), whereas

domain-specific processes seemed not to be affected. Patients in early dementia have an obvious impairment in the central executive system, which was implicated by loss of synchrony between brain regions, but the phonological loop system, represented by Broca's areas, was shown by positron emission tomography (PET) as intact at the same time (Morris, 1994). Patients with very mild AD had difficulty in learning and maintaining words in the middle part of the word list (interfered by both former and latter words) rather than the words in the beginning of the list (Hashimoto *et al.*, 2004). This fact implied a functional deficit of the central executive system. Patients with AD suffered from prominent impairments in the shifting and division of attention (Parasuraman & Haxby, 1993). The first cognitive indicator of neocortical dysfunction in early AD is attentional dysfunction. Disconnection between frontal and posterior parietal areas might be the cause of attentional dysfunction in AD (Clark, Iversen, & Goodwin, 2001). By using tasks selected primarily for the detection of localized neural disruption within PFC, deficits in sustained attention and verbal learning were best indicators of manic performance rather than deficits on any of the tests of executive functioning. In patients with frontotemporal dementia, the activation gain with increasing memory loads was even more decreased than those with AD, but cerebellar activation increased in compensation (Rombouts *et al.*, 2003).

Due to dysfunction of the frontal lobe, non-demented patients with mild

Parkinson's disease had insufficient mental resources for the central executive to use and caused poor performance in a dual-task paradigm (Fournet, Moreaud, Roulin, Naegele, & Pellat, 2000). The assessment for the central executive, for example, the visual memory span backwards, was able to predict dementia severity such as clinical dementia rating (CDR) (Cherry, Buckwalter, & Henderson, 1996). Patients of multiple sclerosis with a working memory problem usually reflected an impaired central executive system (D'Esposito *et al.*, 1996). A study on multiple sclerosis patients using an auditory N-back task and a task with a significant central executive component revealed that the primary working memory impairment in multiple sclerosis patients was within the central executive rather than the phonological loop (Lengenfelder, Chiaravalloti, Ricker, & DeLuca, 2003). Greater cautiousness and increased mental effort were found in closed head injury patients recovered from posttraumatic amnesia (Veltman, Brouwer, van Zomeren, & van Wolffelaar, 1996). Central executive resources reduced in schizophrenia (Granholm, Morris, Sarkin, Asarnow, & Jeste, 1997). Schizophrenia patients showed impairment on both the forward digit span task, a measure of general attention, and the backward digit span task, a measure of verbal working memory (Conklin, Curtis, Katsanis, & Iacono, 2000). Their non-psychotic relatives showed only impairment on the backward digit span task. Working memory dysfunction in schizophrenia patients was due to

DLPFC dysfunction (Perlstein, Carter, Noll, & Cohen, 2001). The pattern of performance was not associated with storage but was related to executive functions. An fMRI study on schizophrenia patients showed that the DLPFC activation decreased and VLPFC activation increased in the manipulation plus maintenance verbal task (Tan *et al.*, 2005). Manipulation was more affected in schizophrenia patients. In clinically stable patients, left DLPFC and right cerebellum were still under-activated and left cerebellum, medial frontal, anterior cingulated and left parietal cortices were still over-activated (Mendrek *et al.*, 2005). Schizophrenia patients who performed an N-back task used greater prefrontal resources but achieved lower accuracy (Callicott *et al.*, 2003). Prefrontal-parietal functional disconnection, prefrontal dissociation and abnormal prefrontal-parietal interaction were found during working memory processing in schizophrenia patients (Kim *et al.*, 2003). A PET study found that schizophrenia patients' performance in working memory tasks was vulnerable to high memory load, along with a reduction of blood flow in right DLPFC (Carter *et al.*, 1998).

1.3.4. Visuospatial processing

1.3.4.1. Visuospatial attention and control

Present experimental results suggest that at least two distinct spatial attentional

systems exist in the brain. A case report of a patient who experienced two successive strokes in the right hemisphere showed that stimulus-centered left neglect happened after the first stroke but body-centered left neglect occurred after the second stroke (Ota *et al.*, 2003). A study on visual neglect patients found that frequent re-fixating of targets by patients might be due to a lateral bias combined with impairment of spatial working memory for the fixation point (Husain *et al.*, 2001). A phenomenon termed the attentional blink, which refers to the detection or discrimination of the second of two successive targets in a rapid serial visual presentation task was often temporarily impaired (Olivers, 2004). It was suggested to be due to spatial compression, a systematic localization bias toward the fovea. During spatial rehearsal, attention was oriented toward the target locations, which was evidenced by increases in visual processing efficiency for these locations (Awh *et al.*, 1998). The increases were not found in a non-spatial memory task using identical stimuli. When participants' attention to memorized locations was blocked, spatial working memory was impaired. ERP modulations during spatial attention start about 80 ms after stimulus onset whereas non-spatial visual attention starts about 100-150 ms post onset (Hillyard, 1998). A sequence-learning experiment that investigated interference between relevant objective information and irrelevant location suggested that sequence learning requires endogenous attention (Deroost &

Soetens, 2006). The participant has to fight automatically captured attention and leads to longer response time. Threat-evoked anxiety and spatial working memory shared a common visuospatial attention mechanism (Lavric, Rippon, & Gray, 2003). A threat of shock was present or absent while performing spatial or verbal N-back tasks. Anxiety was measured by heart rate. The results revealed that anxiety blocked performance of spatial tasks but had no influence on verbal tasks.

1.3.4.2. ERP time course effects associated with visuospatial processing

An EEG study evaluating the peak latency of the posterior contralateral negativity suggested that the time spent in the brain was proportional to the response time in attentional cueing tasks and stimulus localization tasks, but the effect was weaker in visual search (Wolber & Wascher, 2005). A study that applied transcranial magnetic stimulation over the right posterior parietal cortex at different latencies during a visuospatial task suggested that the effective interference occurred at an early stage of 50 ms post-stimulus, which provided the accurate time course for visuospatial processing that the right posterior parietal cortex contributes (Pourtois, Vandermeeren, Olivier, & de Gelder, 2001).

TMS on the bilateral middle temporal area increased reaction time in the visuo-object task, whereas those on bilateral parietal areas increased reaction time in

the visuospatial task (Oliveri *et al.*, 2001). The interference was most evident at the latency of 300 ms in both middle temporal and parietal areas. TMS on the superior frontal gyrus increased response time in visuospatial working memory task, whereas those on the DLPFC increased response time and error rate in both tasks. The interference was most evident at the latency of 600 ms rather than 300 ms in both superior frontal gyrus and DLPFC areas. These findings suggested that there are separate buffers for object and spatial working memory in the posterior, and DLPFC for the executive functions regardless of the stimulus types.

1.3.4.3. Spatial-object dichotomy

The disruption of a visual working memory task from visual interference was stronger than the one from spatial interference, whereas the disruption of a spatial working memory task from spatial interference was also stronger than the one from visual interference (Klauer & Zhao, 2004). This phenomenon suggested that visuospatial working memory should be divided into separate visual and spatial components. The fact that spatial working memory could be interfered with in the encoding stage by irrelevant location information also suggested dissociation of spatial and object memory (Hale, Myerson, Rhee, Weiss, & Abrams, 1996). A study of the performance difference between Chinese and Caucasian participants on working

memory tasks reported that in the initial learning tasks Chinese participants tended to activate the dorsal stream for spatial feature analysis, whereas Caucasians tended to recruit the ventral stream for object identification (Gron, Schul, Bretschneider, Wunderlich, & Riepe, 2003).

1.3.4.4. Anatomical relationships

The right hemisphere is associated with global-level processing and spatial coordinate judgments, whereas the left hemisphere is associated with intact local and categorical judgments (Schatz, Craft, Koby, & DeBaun, 2004). A study on two callosotomy patients revealed right-hemisphere superiority for spatial judgements and left-hemisphere superiority for identity judgments (Corballis, Funnell, & Gazzaniga, 1999). Persons with atypical right hemispheric dominance for language have more bilateral activation during spatial judgment than typical persons (Jansen, Floel, Menke, Kanowski, & Knecht, 2005).

A study on monkeys with lesions of areas 9 and 46 in DLPFC reported that egocentric spatial memory which refers to the map from their own viewpoint was impaired but allocentric spatial memory which refers to memory of a 3D environmental map was intact (Ma, Tian, & Wilson, 2003). Prefrontal neurons related to stimulus identity were different by function and region from neurons related to stimulus location (Wilson, Scalaidhe, & Goldman-Rakic, 1993). A study on

patients with intracranial tumour after resection also revealed that object memory and positional memory were separate systems (Kessels, Postma, Kappelle, & de Haan, 2000). Spatial memory problems existed in patients with lesions in either posterior parietal lobe or in the right hemisphere. An fMRI study for a facial working memory task presented that three occipitotemporal areas responded transiently to stimuli indicated perceptual processing (Courtney, Ungerleider, Keil, & Haxby, 1997), whereas sustained response in three prefrontal areas suggested working memory. Different degrees of selectivity in visual areas and different strengths of sustained activity in prefrontal areas revealed a functional specialization from occipital to prefrontal areas. Another fMRI study on children using a spatial working memory task (Nelson *et al.*, 2000) reported that subtraction of the activation of the motor condition from the memory condition revealed activity in the dorsal PFC and in the posterior parietal and anterior cingulate cortex. A study using repetitive TMS to block the DLPFC (Robertson, Tormos, Maeda, & Pascual-Leone, 2001) revealed that learning of position were also blocked but object learning was preserved. This effect could not be found in the similar TMS treatment on parietal lobes. These results suggested that DLPFC plays an important role in spatial working memory.

The right posterior parietal cortex (PPC) was implicated in visuospatial processing by studying patients with visuospatial neglect (Pourtois *et al.*, 2001). A

study on right hemisphere stroke patients with and without hemineglect (Malhotra *et al.*, 2005) showed that spatial working memory capacity was correlated with severity of left neglect, and the anatomy findings of lesion in the parietal white matter and insula. In a mental rotation task, female participants presented strong right-lateralized ERP bias when making non-dominant hand responses (Johnson, McKenzie, & Hamm, 2002). Male participants showed a right parietal bias regardless of response hand. The results suggested the importance of considering the factors of sex and handedness in a spatial manipulation task.

The anterior thalamic nuclei and the hippocampus were critical areas for spatial memory and work dependently during the performance of certain spatial learning tasks (Henry, Petrides, St-Laurent, & Sziklas, 2004). An animal study showed that mice with hippocampal rather than parietal cortex lesion had deficits in measuring egocentric distance and place map, which implies that the hippocampus appears to be involved in working memory for egocentric distance and spatial location information, whereas the parietal cortex was not (Long & Kesner, 1998). A study surveying children with chromosome 22q11.2 deletion syndrome suggested that the significant reduction of thalamus, including the pulvinar nucleus, causes visuospatial deficits in this group (Bish, Nguyen, Ding, Ferrante, & Simon, 2004). An MEG study using a spatial working memory task and more perceptual tasks for comparison reported that

the MTL showed sustained activation from 200 to 800 ms post-stimulus in a spatial working memory task, whereas the activation sustained from 200 to 400 ms post-stimulus in perceptual tasks (Campo, Maestu, Capilla *et al.*, 2005). In the period 200 to 400 ms post-stimulus, both tasks presented the same activation. This result suggests that pure encoding starts only after 400 ms post-stimulus. A study on temporal lobectomy patients reported that the right anterior temporal lobe stores long-term allocentric spatial memory for the reference of spatial working memory (Feigenbaum & Morris, 2004).

1.3.5. Verbal processing

1.3.5.1. Anatomical relationships

Verbal working memory is generally thought to be housed in a left-dominant neural network, including parietal, temporal and PFC. An evoked-potential study on aphasic patients reported that in normal persons and non-aphasic brain-injured patients the left hemisphere was activated during a verbal memory task, whereas in recovered aphasics the right hemisphere was activated (Papanicolaou, Levin, & Eisenberg, 1984). Left parietal and right frontal positivities are usually observed by ERP studies in verbal recognition tasks (Graham & Cabeza, 2001). For non-verbal emotional stimuli, left frontal effect was noted for happy faces, and a right frontal

effect was noted for neutral faces. The parietal positivities could not be seen in non-verbal stimuli, implying that the left lateralization of parietal activities reflected verbal processing.

A study using repetitive TMS during and after the performance of a verbal working memory task suggested a symmetrical, bilateral parietofrontal verbal working memory network (Mottaghy, Doring, Muller-Gartner, Topper, & Krause, 2002). The result was explained as a parietofrontal central executive network during the processing of semantic and objective features. Verbal working memory performance activated Broca's area, the left premotor cortex, the cortex along the left intraparietal sulcus and the right cerebellum (Gruber, 2001). After silent articulatory suppression that blocked the participant's rehearsal, no significant memory-related activation was found in these areas. However, non-articulatory maintenance occurred instead in anterior prefrontal and inferior parietal lobes. An fMRI study suggested that rehearsal was optional but encoding was an obligatory component of the phonological loop, which is located in the left inferior frontal gyrus, right lateral cerebellum and medial frontal gyrus (Li *et al.*, 2004). Another fMRI study using a sentence-pair matching task revealed that left dorsal frontal and left inferior parietal regions were more activated with increasing memory load. The left parietal lobe was involved in semantic matches, whereas the left ventral frontal lobe was involved

in mismatches (D'Arcy, Ryner, Richter, Service, & Connolly, 2004).

1.3.5.2. Word and sentence processing

An fMRI study on verbal working memory revealed that supplementary motor, premotor and inferior frontal areas are associated with maintenance, and left inferior frontal and supplementary motor regions are associated with articulatory rehearsal (Chein & Fiez, 2001). Another fMRI study on Chinese reading in dyslexia patients revealed that both the processes from orthography to syllable and from orthography to semantics involve left middle frontal gyrus (Siok, Perfetti, Jin, & Tan, 2004). An ERP study also on Chinese reading found that N2 on the right anterolateral scalp in the time window 182-240 ms post-stimulus was significantly larger for target stimuli in the visual word recognition task, whereas the N2 on the left anterolateral scalp in the time window 262-350 ms post-stimulus was larger for non-target stimuli (Wang, Tang, Kong, Zhuang, & Li, 1998).

Sentence comprehension involves the posterior middle and superior temporal gyri which process sentence structure, the anterior temporal gyrus which processes sentence context, and left inferior frontal cortex which supports verbal working memory for lexical item processing (Stowe *et al.*, 1998). A sentence memory study using N-back tasks and composite complex span score suggested that the sentence

memory task is related to different working memory modules (Roberts & Gibson, 2002). A PET study showed that sentence listening activated the bilateral superior and middle temporal gyri but left side activation was stronger. Sentence generation involved the left middle and inferior frontal gyri, and left inferior temporal lobe (R.-A. Muller *et al.*, 1997). An fMRI study on schizophrenia patients suggested that activation in the left inferior frontal gyrus is reduced in patients with verbal working memory deficits (Stevens, Goldman-Rakic, Gore, Fulbright, & Wexler, 1998).

1.4. Laboratory tasks and sub-processes of WM

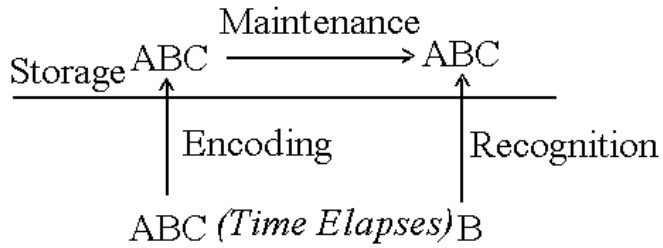

Figure 1-1 *Logical analyses of item-recognition tasks*

1.4.1. Item-recognition tasks and the traditional model: encoding, active maintenance and recognition

Item-recognition tasks (Ruchkin, Johnson, Grafman, Canoune, & Ritter, 1992;

Sternberg, 1966) comprise of clear-cut stages of encoding, maintenance and recognition (See Figure 1-1) and reflect the traditional model of encoding-storage-retrieval processes. Encoding is a conscious process which transfers and screens physical information into relevant neural signals. Active maintenance is conscious processes keeping neural signals alive. Recognition is the stage that compares the retrieved memory with the target and generates task performance indices, namely response time and error. However, not every WM task has clear steps of encoding, active maintenance and recognition, for example, N-back tasks, which mix these steps together.

1.4.1.1. Experimental evidence of the proposed sub-processes

An ERP study of an item-recognition task (Ruchkin *et al.*, 1992) required participants to memorize items in the beginning and then recognize them later. It showed that domain-specific differences occurred in early ERPs in the posterior N220 component, and a phonological loading effect was found at the P300 component by increasing amplitudes with increasing loads, but visuospatial loading effects were not found at the same latency. The encoding period for visuospatial stimuli started by an abrupt *topographic transition* at 750 ms post-stimulus and kept similarity until the end of the recording epoch. This also suggested a more direct transition from sensory input to

maintenance rehearsal, with a significant shift in lateralization from right dominant to the midline in the retention interval. The topographic transition at 600, 1000 and 3000 ms post-stimulus marked the more complex encoding activity of the phonological task.

1.4.2. N-back tasks: information manipulation and executive functions

Although the traditional encoding-storage-retrieval model is broadly assumed in memory research, the stepwise computational model is criticized because the components are chosen arbitrarily and represents merely a computational account that may not reflect actual human memory (Malafouris, 2005; O'Reilly, Braver, & Cohen, 1997; Riegler, 2005). The N-back tasks provide another viewpoint for working memory, which has been commonly used in electrophysiological and imaging studies on WM (Gevins & Cutillo, 1993; Jansma, Ramsey, Coppola, & Kahn, 2000; Smith & Jonides, 1997).

1.4.1.1. Task description

In the N-back task, the participant is shown a series of items (e.g., letters, words or location markers) and is asked to decide, upon presentation of each item, whether a given property of the current item matches the same property of the item n

presentations back. Figure 1 displays a schematic diagram of the 0-, 1- and 2-back tasks. If n = 0, each new item is matched against the very first item in the series. If n = 1, each new item is matched against the immediately preceding item, and if n = 2, the new item is matched against the item presented just before the preceding item.

Researchers currently prefer the N-back task in studies of WM because it taps into processes involving manipulation as well as maintenance of information in WM. (e.g., Meegan, Purc-Stephenson, Honsberger, & Topan, 2004; Ragland *et al.*, 2002). Impairment in executive function of WM is suggested as a feature of early Alzheimer's dementia (Hashimoto *et al.*, 2004; Morris, 1994; Vecchi & Cornoldi, 1999; Vecchi, Saveriano, & Paciaroni, 1998), and, in these patients, continuous deterioration of WM performance is noted in dual rather than single task settings (Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991). Thus, a clear delineation of WM processes is important from both theoretical and clinical points of view.

1.4.2.2. Experimental evidence from N-back tasks

Intuitively, matching and other WM manipulations in N-back tasks are simultaneous. An event-related potential (ERP) study found that P300 latency was constant with increasing N but P300 amplitudes increased with increasing N (Watter, Geffen, & Geffen, 2001). Latency of P300 reflects performance of matching (the quicker the

better) whereas P300 amplitude reflects attention and memory loading (the larger the harder). As a result, the N-back task is considered a dual task with parametrically increasing attentional and memory loading along with constant loading of an implanted matching subtask. Because matching load is purportedly constant, matching effects can be potentially eliminated by comparing different N-back tasks, and memory effects clarified.

1.4.2.3. What is lacking in previous studies using the N-back task?

Although N-back tasks are broadly used in WM studies, its sub-processes have not been sufficiently elucidated. It has been suggested, however, that the literature in fact lacks a thorough task analysis of the N-back paradigm, and that this leaves room for seemingly reasonable assumptions that may prove to be unsustainable under closer inspection. For example, task analysis (Meegan, Purc-Stephenson, Honsberger, & Topan, 2004) has cast doubt on the commonly held assumption that spatial and verbal N-back tasks actually tap into spatial and verbal WM processes, respectively. Based on behavioral studies using letter and position N-back tasks, these authors concluded that irrespective of the actual stimulus material or task demands, N-back task performance always involves both spatial and verbal processing (See also Meegan & Honsberger, 2005). This conclusion fits with neuroimaging results (Smith &

Jonides, 1997) showing that in an N-back task where letters were presented at different positions, activity in both cerebral hemispheres was obtained both under verbal task instructions (matching letter identity) and under spatial task instructions (matching letter position). However, because activity was lateralized slightly to the left under verbal instructions, and slightly to the right – at least in some areas – under spatial instructions, these authors concluded that verbal and spatial WM are in fact mediated by different neural substrates. Because temporal resolution was too low to analyze sub-processes in previous imaging studies (Ragland *et al.*, 2002; Smith & Jonides, 1997), earlier studies revealed only summation of overlapped sub-processes during a particular long period.

1.5. Imaging and electrophysiological methods in working memory research

Modern technology enables us to show brain activity directly. Here I compare PET, fMRI, EEG and ERPs and elaborate on ERPs.

1.5.1. PET

This method applies radioactive isotopes (usually Xe133) to label blood molecules. When a brain area is activated, it will metabolise more, thus more radiation will be

detected. PET has excellent topographical resolution of a few millimetres (Aguirre, 2003). However, it has very poor temporal resolution limited by the half-life of the radioisotope used. It limits the ability of the method to dynamically track changes in neural activity related to cognitive processes.

1.5.2. fMRI

Functional MRI is based on the increase in blood flow to the local vasculature that accompanies neural activity in the brain. This results in a corresponding local reduction in deoxyhemoglobin because the increase in blood flow occurs without an increase of similar magnitude in oxygen extraction (Fox and Raichle, 1985). fMRI has good spatial and temporal resolution. Because it can provide real-time information, an event-related fMRI is often applied in cognitive psychology experiments. A problem is that fMRI is expensive. Furthermore, although the temporal resolution of fMRI is higher than PET, it is not high enough for psychological responses that occur at the level of a few milliseconds. Also, participants need to keep steady during testing to avoid motion artifacts.

1.5.3. EEG

Electrophysiological tools provide excellent temporal resolution at the level of milliseconds. However, the spatial resolution is poor. EEG involves recording

electrical potentials at the scalp, and is suggested to reflect the activity of the cortex below the electrodes. The analysis of EEG is usually frequency and amplitude-based. Electrical pulses from muscles, (for example, eye-blinking) usually cause artifacts. Magnetoencephalogram (MEG) records magnetic field instead of voltages and provides higher spatial resolution than EEG. ERPs are EEG per se with further processing.

1.5.4. ERPs

ERPs are superimposed time-locked EEG epochs. Therefore, peaks, wave troughs and noises are neutralized in ERPs. ERPs provide more detailed temporal information of the underlying processes involving in a task. It actually offers the best temporal resolution of all imaging techniques. The main limitation is that it needs multiple presentations of stimuli. Furthermore, disadvantages in EEG, for example, vulnerability to muscle artifacts and poor spatial resolution, also exist in ERPs.

The traditional task inducing ERP components is the oddball paradigm. The most discussed ERP components are P3 (P300), whereas N1, P2 and N2 have also been discussed for more than 20 years (Knight, Hillyard, Woods, & Neville, 1981; Naatanen, 1979; Perrault & Picton, 1984a, , 1984b; Renault, Ragot, Lesevre, &

Remond, 1982; Ritter, Simson, & Vaughan, 1983; Woods, Clayworth, Knight, Simpson, & Naeser, 1987). A method usually applied to augment P3 is to provide target instruction before the oddball paradigm (Chapman & Bragdon, 1964; Donchin & Cohen, 1967; Picton & Hillyard, 1974). A recent ERP study showed that a central negativity peaking at 300 ms (N2) was enhanced by novel stimuli predicting a target, and P3a and P3b were reduced at the same time (Suwazono, Machado, & Knight, 2000). As the prediction rate fell, the N2 amplitudes decreased but P3a and P3b amplitudes increased. Another ERP study (Potts, Patel, & Azzam, 2004) suggested that P1 and N1 (about 200 ms post-stimulus) was enhanced by instruction orienting to infrequent stimuli. A prefrontal positivity (P2a, about 200 ms post-stimulus) was enhanced in response to instructed targets. P300 was enhanced to the infrequent stimuli rather than to target instruction. In conclusion, components in ERPs recorded during the target-instructional oddball paradigm can be summarized as: P1 and N1 (posterior deflections about 200 ms post-stimulus) are usually enhanced by attentional instruction before the task; P2a (a frontal positivity about 300 ms post-stimulus), N2a (a frontal negativity about 300 ms post-stimulus) and P3 (a posterior positivity about 400 ms post-stimulus) are enhanced in response to an instructed target, although P3 was also reported enhanced by infrequency (Eimer, 1997; Herron, Quayle, & Rugg, 2003; M. M. Muller & Hillyard, 2000; O'Donnell,

Swearer, Smith, Hokama, & McCarley, 1997; Potts et al., 2004; Suwazono et al., 2000)

1.6. The Present Work

1.6.1. The aims of this thesis

In this thesis, I will present a new logical analysis of the structure of the N-back task (see Section 1.5.2), and test its predictions in two ERP experiments, the first conceptually driven, and the second data-driven.

In addition to N-back task sub-processes, the thesis will focus particularly on the issue of spatial-verbal dichotomy (See Section 1.3.1) and try to find relationships between WM components and the N-back task's sub-processes.

1.6.2. Proposed logical analysis of the N-back task sub-processes

In N-back tasks, there are no clear-cut stages of encoding, active maintenance and recognition. Instead, by logical analysis, matching, replacement and shift exist at different levels of N-back tasks (See Figure 1-2). Matching is close to recognition in item-recognition tasks, but exists in the beginning rather than the end of the task and integrates perceptual and memorizing (encoding-equivalent) processes.

Replacement is the interface between the external environment and the internal buffer, which has some encoding and maintenance function. Shift is the internal replacement without the encoding component and reflects an executive function more than those in item-recognition tasks.

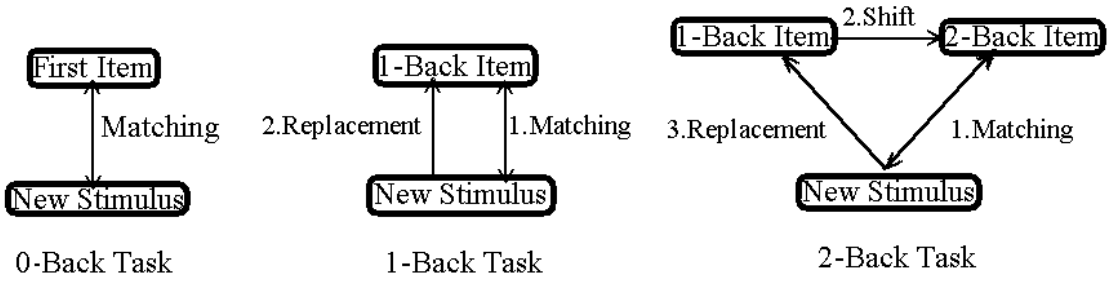

Figure 1-2 *Logical analyses of N-back tasks*

A schematic representation of the processes involved in N-back tasks is provided in Figure 1-2. At all values of N, the task requires that (a) each stimulus (item) in the presented series is *encoded*, (b) a representation of the target stimulus is *maintained* in memory, and (c) each item-representation is *matched* against this stored representation of the target. However, information maintenance and manipulation load changes systematically as the value of n increases.

In the 0-back task, the participant needs to maintain only one item (i.e., the very first one in the series) in memory. In the 1-back task also, the participant similarly needs to maintain only one item (i.e., the previous one) in memory – in addition, however, this task requires the regular *updating* of WM, as each new stimulus *replaces* the old 1-back item to become the new matching target. In the 2-back task,

the participant needs to maintain two items in memory (i.e., two stimuli preceding the current one), and also needs to keep track of their respective order. Correspondingly, WM updating is not a 1-step replacement, but a 2-step *shift and replacement* operation: After matching against the newly presented item, the current 1-back item is shifted to the 2-back position ('shift'), and the current item replaces the contents of the 1-back position ('replacement').

Thus, in terms of information *maintenance* requirements, the 0-back and 1-back tasks carry the same load of one item, but the 2-back task carries a greater load of two items plus order information. On this basis, we may expect that any experimental effects that are purely a function of changing maintenance load should only differentiate the 2-back task from the 0-back and 1-back tasks. On the other hand, effects that are due to changes in the *updating* process (no updating versus 1-step replacement versus 2-step shift & replacement) should differentiate each of these three conditions. In particular, ERP and performance differences between 1-back and 0-back conditions are likely to reflect the 1-step target replacement operation, whereas differences between the 2-back and 1-back conditions are likely to reflect both increased maintenance load as well as increased updating requirement.

The replacement sub-process is the "reception window" of external information (see Figure 1-2). In contrast, because the shift sub-process is logically isolated from

external stimuli (see also Figure 1-2) and the manipulated material in the shift sub-process is already located in WM storage, shift is also considered "internal replacement". Replacement is hypothetically influenced directly by bottom-up control in the posterior area, whereas shift is influenced primarily by top-down control in the frontal area (e.g., Courtney *et al.*, 1997; Halgren *et al.*, 2002; Kessler & Kiefer, 2005; Pourtois *et al.*, 2001). This hypothesis is consistent with Andres & Van der Linden (2002) and Baddeley *et al.* (1997), where executive processes were not exclusively sustained in the frontal cortex.

Hemispheric lateralization is known to exist in domain-specific tasks (e.g., spatial vs. verbal), in general processing (e.g., Beauregard, Chertkow, Murtha, Dixon, & Evans, 1997; Deutsch, Bourbon, Papanicolaou, & Eisenberg, 1988; Petersen, Fox, Snyder, & Raichle, 1990), between levels of n in N-back tasks (e.g., Smith & Jonides, 1997), or by identical stimuli whose domains were assigned by top-down control (Stephan *et al.*, 2003). The N-back task allows interface customization in the sense that domain-specific tasks can be created either by conceptual or data-driven control. In a conceptual N-back task, different attributes of apparently identical stimuli can be rendered relevant by different task instructions. Because only instructions differ between the spatial and verbal versions of the task, domain-specific lateralization should be expected in the shift sub-process, which is supposedly influenced by

conceptual control. However, domain-specific lateralization should not be expected in the replacement sub-process, which is purportedly a data-driven sub-process (and the appearance of stimuli is identical in both versions). In the contrasting design of data-driven N-back tasks, attributes relevant to the task are defined by stimulus appearance, and therefore domain-specific lateralization should be expected in the replacement process.

1.6.3. Proposed experimental tests of the logical analysis

Sub-processes of the N-back task were tracked using difference waveforms: 1-back – 0-back waveforms containing the replacement sub-process, and 2-back – 1-back waveforms containing the shift sub-process.

1.6.4. Choice of ERP as methodology

Because temporal resolution was too low to analyze sub-processes in previous imaging studies (Ragland *et al.*, 2002; Smith & Jonides, 1997), these studies revealed only summation of overlapped sub-processes during a particular (long) period. For this reason, the current study applied ERP, which has high temporal resolution, to scrutinize sub-processes of the N-back task.

1.7. Overview of the following chapters

The following chapters describe details of experiments.

1.7.1. Chapter 2

Experiment 1, which studied the spatial-verbal dichotomy, was performed under top-down (conceptual) control. Differences and similarities between verbal and spatial WM tasks were investigated using event-related brain potentials (ERPs) and behavioral measures. Using an N-back task with three levels of N (0-, 1-, and 2-back), participants matched the identity (verbal task) or the position (spatial task) of words against a target word. Stimulus display was identical under both task instructions. A systematic task analysis suggested that in addition to matching processes, replacement of the target item and shift from latent to actual target were relevant sub-processes of the N-back task, and that the latter two distinguished between levels of N. Systematic differences between spatial and verbal tasks were obtained for all three sub-processes, but clear evidence of lateralization was found only for the shift process. However, the basic assumption that identical stimuli are perceptually identical remained un-tested. Thus, Experiment 2 was needed to know whether the spatial-verbal difference was due to task processes per se or not.

1.7.2. Chapter 3

Experiment 2 aimed at selective attention under a conceptually-controlled N-back task. Selective attention and interference from irrelevant domains are frequently neglected factors in working memory experiments. Here N-back tasks were employed with identical stimuli under spatial and verbal task instructions. Information from the irrelevant domain was found to systematically affect processing in the relevant domain. The results highlight the importance of taking cross-domain interfering factors into account when drawing conclusions from neuropsychological experiments, and suggest that Experiment 1 did not "purely" compare spatial and verbal effects but increased interference from selective attention. An experiment with data-driven (bottom-up) control, which has different stimuli between spatial and verbal tasks, is thus needed.

1.7.3. Chapter 4

Experiment 3 is therefore the corresponding one of Experiment 1 but designed by data-driven control. The spatial-verbal dichotomy of working memory (WM) tasks was investigated using event-related potentials (ERPs). Using an N-back task with three levels of n (0-, 1-, and 2-back), participants either matched words presented at a fixed screen position (verbal task) or they matched the locations of non-word symbols

presented at various positions across the screen (spatial task). A systematic task analysis showed that in addition to perceptual matching processes, replacement of the target item and shift from latent to actual target were relevant sub-processes of the N-back task, and that the latter two distinguished between levels of n. Systematic differences between spatial and verbal tasks were obtained for all three sub-processes, but domain-specific lateralization was only found in replacement.

Chapter 2. Experiment 1: Is information processing different under spatial and verbal instructions?

2.1. Introduction

Experiment 1 aimed to provide a fine-grained analysis of the electrophysiological correlates of verbal versus spatial WM processes during an N-back task. Identifying the neural correlates of WM in the N-back task will become easier and more reliable if our assumptions about the cognitive operations required for manipulating information in this task are clearly delineated and tested. To this purpose, ERPs elicited under spatial and verbal task instructions in 0-, 1- and 2-back conditions were compared. Therefore, not only spatial-verbal dichotomy in general processing, but also in logically sub-processes is delineated. With the excellent temporal resolution, ERPs were applied to isolate and compare the (broadly localized) electrophysiological correlates of these sub-processes under verbal versus spatial task instructions.

It has to be noted that any systematic differences in perceptual processing across the spatial and verbal versions of the task would cause corresponding differences in early ERP components, and might also produce corresponding follow-up differences in later components (e.g., Schendan, Ganis, & Kutas, 1998). Therefore, such perceptual differences were eliminated by employing identical stimulus displays in both tasks and changing only the task instructions. Stimuli were drawn from lists of 20 words and were presented one at a time at one out of eight different screen locations. Under *spatial task instructions*, participants were asked to

match the screen location of items. Under *verbal task instructions*, they were asked to match word identity.

Data analysis proceeded in two steps. First, general patterns of ERP effects were examined associated with the spatial and verbal tasks. I expected to replicate earlier findings such as an increased posterior P3 amplitude for infrequent 'match' relative to frequent 'non-match' trials (e.g., Katayama & Polich, 1999), and reduced P3 amplitude under higher WM load conditions (e.g., McEvoy, Smith, & Gevins, 1998b). The question of interest was how task instructions (spatial versus verbal) would alter the processing of identical stimulus displays. An imaging study using identical stimuli under domain-specific instructions (Stephan *et al.*, 2003) suggested that the verbal task should be accompanied by neural activity predominantly in the left hemisphere, whereas the spatial task should be accompanied by neural activity predominantly in the right hemisphere.

Second, specific differences in ERP patterns between the sub-processes of the N-back task were examined. Based on the task analysis presented above, I expected ERP differences between 1-back and 0-back conditions to specifically reflect the physiological correlates of the replacement operation, and differences between the 2-back and 1-back conditions to reflect effects of shift operation. Again, to the extent that task instructions elicited domain-specific processing, these effects should

show hemispheric lateralization (Smith & Jonides, 1997).

2.2. Method

2.2.1. Participants

Sixty paid volunteers (35 female) ranging in age from 18 to 40 (mean 21) years participated in the experiment. According to self-report, all had normal or corrected-to-normal vision, and all except six participants were right-handed.

2.2.2. Stimulus and apparatus

Stimulus presentation and data acquisition were managed by C-programs and running under MS-DOS. Behavioral and affect data were saved on the hard disc.

Stimuli were 20 words with similar frequency and length. Words were presented in white on black on a 17" computer monitor, at one out of eight circularly arranged positions 4° from the screen centre. Words had a height of approximately 0.8° visual angle, and the width ranged from 3.2° to 6.4° (mean: 5°).

2.2.3. Procedure

Participants were seated in an armchair in front of a computer screen at distance of

approximately 60 cm. They were told to keep a comfortable posture, and to avoid eye movements and eye blinks during experimental trials.

2.2.3.1. Experimental steps

Participants completed the first half of the main experiment, comprising six blocks of N-back tasks, followed by a break, during which participants were encouraged to leave the experimental room. They then completed the second half the main experiment.

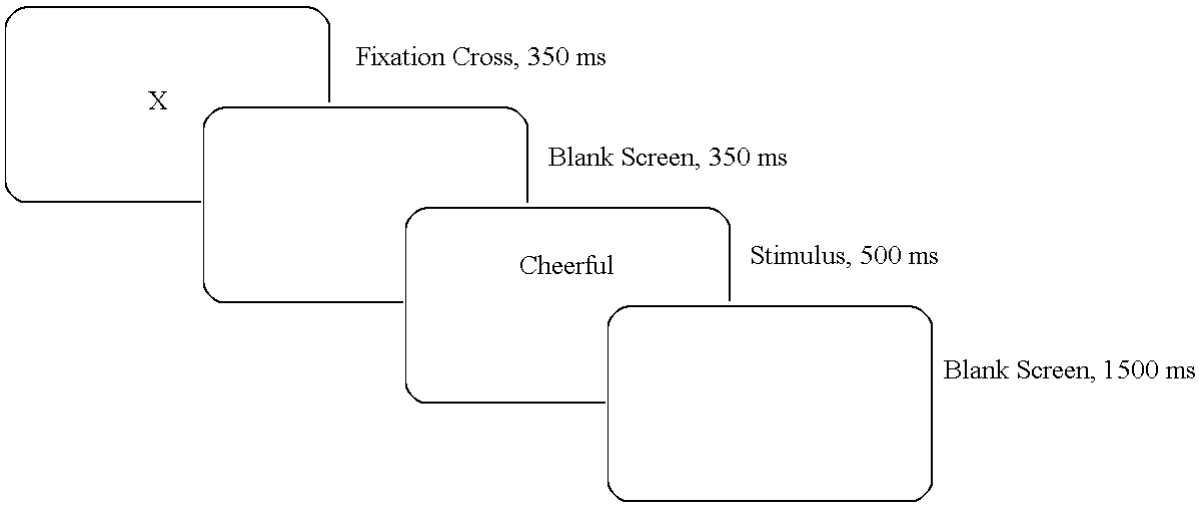

Figure 2-2. *An experimental trial*

Each half of the main experiment consisted of two 0-back blocks, two 1-back blocks, and two 2-back blocks in sequence. In the first experimental half, each pair

of blocks was preceded by a corresponding practice block, to familiarize participants with the changing task requirements. In the second half, no practice blocks were administered. Experimental blocks consisted of 64 trials (20 target trials and 44 non-target trials). Each trial began with the presentation of a fixation cross in the centre of a screen for 350 ms, followed by 350 ms of a blank screen. Then a stimulus word was shown for 500 ms at one of the eight predefined screen locations. This was followed by another blank screen for 1500 ms (see Figure 2-2). In all blocks, identity and location of each stimulus were determined pseudo-randomly, to achieve an approximately even distribution of targets and an approximately equal distribution of identities and locations. Practice blocks were constructed in the same way, but contained only 20 trials and provided additional feedback (the words "correct" or "wrong" presented in the centre of the screen) immediately after the participant's response. Data from practice blocks was not saved.

In the 0-back task, participants indicated whether or not each stimulus matched the first one of the block. For the more demanding levels of the N-back task, participants had to match the current stimulus with the previous stimulus (1-back task) or the stimulus before the previous one (2-back task). Participants pressed a "yes" key for a match (target stimulus) and a "no" key or a mismatch (non-target stimulus). Keys were "\"and "/" keys of a computer keyboard, which had to be pressed with the

left and right index finger, respectively. Participants were asked to respond as quickly and accurately as possible, and assignment of keys to "yes" and "no" response was counterbalanced across participants.

2.2.3.2. Experimental groups

Two different versions of the N-back task were employed, and participants were assigned randomly to either of these. In the *verbal version*, the task-relevant feature of the stimulus words was their identity, whereas their location was irrelevant. In the *spatial version*, the location on the screen was task-relevant, whereas the identity was irrelevant. Note that verbal and spatial versions of the experiment differed only with respect to the instruction given to the participants, and where identical in all other respects.

2.2.4. Electrophysiological recording and data processing

2.2.4.1. Acquisition

Using a BioSemi Active-Two amplifier system, continuous EEG recordings were made with Ag / AgCl electrodes, mounted on a nylon cap, from 32 locations of the international 10–20 system (left: Fp1, AF3, F7, F3, FC1, FC5, T7, C3, CP1, CP5, P7,

P3, PO3, O1; midline: FZ, CZ, PZ,OZ; and corresponding right channels). Sampling rate was 256 Hz. EEG signals were off-line filtered using a 0.01 Hz high pass and a 30 Hz low pass filter, and were re-referenced to linked earlobes. EOG data was not saved. However, it may not be important for interpretation of the frontal amplitudes. It is because stimulus location was random, and participants were not given advance information about it. Therefore, they could not have moved their eyes to the stimulus location in advance except by chance. Furthermore, because of the relatively long inter-trial interval and the onset of a fixation cross at the beginning of each trial, it seems safe to assume that participants did indeed fixate the screen centre at the start of each trial. Once a stimulus appeared on the screen, participants presumably did move their eyes towards it on at least some trials. However, this is true for all trials, regardless of stimulus type (target or non-target) and task instruction (spatial or verbal). Therefore, there doesn't seem to be a way how eye movements could systematically contribute to differences between trial types or tasks.

2.2.4.2. Pre-processing

Further analysis was conducted using EEGLAB 4.43 (Delorme & Makeig, 2004) running under MATLAB 6.1 environment. EEG was averaged off-line for epochs of 900 ms, starting 100 ms prior to stimulus onset, and ending 800 ms afterwards.

Trials containing saccadic eye movement or eye blinks (indicated by amplitudes beyond 3 SD in single channel and 1.5 SD in all channels), and trials where participants gave an incorrect response, were excluded from analysis. EEG on correct-response trials was averaged for each condition separately, relative to a 100-ms pre-stimulus baseline. Thus for each participant, 6 ERP waveforms were constructed: one target ERP and one non-target ERP from each of the 0-, 1-, and 2-back task.

2.2.5. Data analysis

2.2.5.1. Data trimming

Eight participants were excluded because after artifact rejection, they had less than 25 EEG trials remaining in one or more conditions, or they produced error rate of more than 2.5 SDs above the group's mean. No other data trimming procedures were employed.

2.2.5.2. Behavioral data

Response time (RT) and error rate were analyzed using a repeated-measures analysis of variance (ANOVA) with the between-subject Task (spatial, verbal) and the

within-subject factors Stimulus (match, non-match) and N-Back (0, 1, 2).

2.2.5.3. ANOVA of original ERPs

Based on visual inspections of the grand mean waveforms (collapsed across N-Back conditions), four latency windows were selected for analysis: An early (150-250 ms) positive-negative shift in posterior areas (non-midline: P3/4, P7/8, O1/2, PO3/4; midline: Pz, Oz), further referred to as early posterior complex (EPC); a positive peak between 200-300 ms in anterior areas (non-midline: FP1/2, AF3/4, F7/8, FC1/2, FC5/6; midline: Fz, Cz), further referred to as P2a; a negative-going shift at 300-400 ms in anterior areas (non-midline: FC5/6, F7/8, FC1/2, AF3/4, FP1/2; midline: Fz, Cz), further referred to as N2; and a P3 component at 300-500 ms in central-posterior areas (non-midline: FC1, FC5, C3, T7, CP1, CP5, P3, P7, O1, PO3, and corresponding contralateral channels; midline: Cz, Pz, and Oz). ERP component amplitudes, which were defined as mean amplitudes within these time window, were analyzed separately using a repeated-measures ANOVA with the between-subject factors and Task and the within-subject factors Stimulus and N-Back (0 / 1 / 2), and with the additional factor Hemisphere (left / right) in the analysis of non-midline channels.

2.2.5.4. Replacement and shift effects and t-statistical maps

Replacement- and shift effects were defined as mean amplitude differences between 1-back and 0-back conditions ('replacement') and between 2-back and 1-back conditions ('shift'). Difference potentials were supposed to present for sub-processes, which is different from the original waveforms which present for summation of all the processes.

The different intervals were chosen according to the difference waveforms. After the difference procedure, the waveforms became totally different from those in original waveforms. P3 component, which is prominent in original waveforms, is not prominent in difference waveforms.

Based on visual inspections of these difference waveforms, three latency windows were selected for analysis of the hypothesized sub-processes: 200-400, 400-600, and 600-800 ms post stimulus. Within each latency window, the mean amplitude difference was tested against 0 at each individual electrode. After that, t-statistical maps were drawn with every electrode colored with white (significant positive), light grey (non-significant positive), dark grey (non-significant negative) or black (significant negative).

2.2.5.5. ANOVA of replacement and shift

Omnibus ANOVA with the between-subject factor Task and the within-subject factor Hemisphere and ACP (anterior / central / posterior) were conducted separately for each of the latency windows and regions of interest: anterior (F7 / 8, AF3 / 4), central (C3 / 4, T7 / 8), and posterior (P3 / 4, P7 / 8).

An α-level of .05 was applied for all statistical analyses. Greenhouse-Geisser corrections were applied and corrected p-values were reported where appropriate.

2.3. Results

2.3.1. Behavioral data

Figure 2-3 presents behavioral results.

2.3.1.1. Response time

Overall response time to non-target stimuli were longer in spatial tasks and decreased in verbal tasks in comparison with that to target stimuli, which was about the same in both tasks, as evidenced by a significant Stimulus × Task interaction, $F(1, 50) = 8.73$, $p = .005$. Response time were longer with increasing memory loads, as evidenced by a significant N-Back effect, $F(2, 100) = 67.06$, $p < .001$. In 0- and 1-back tasks, RT to non-target stimuli was shorter than that to target ones in 0-back tasks, almost

the same in 1-back tasks, and longer in 2-back tasks, as evidenced by a significant Stimulus × N-Back effect, $F(2, 100) = 16.9$, $p < .001$. Other main effects or interactions were non-significant in RT, all $F < 2.18$, all $p > .138$.

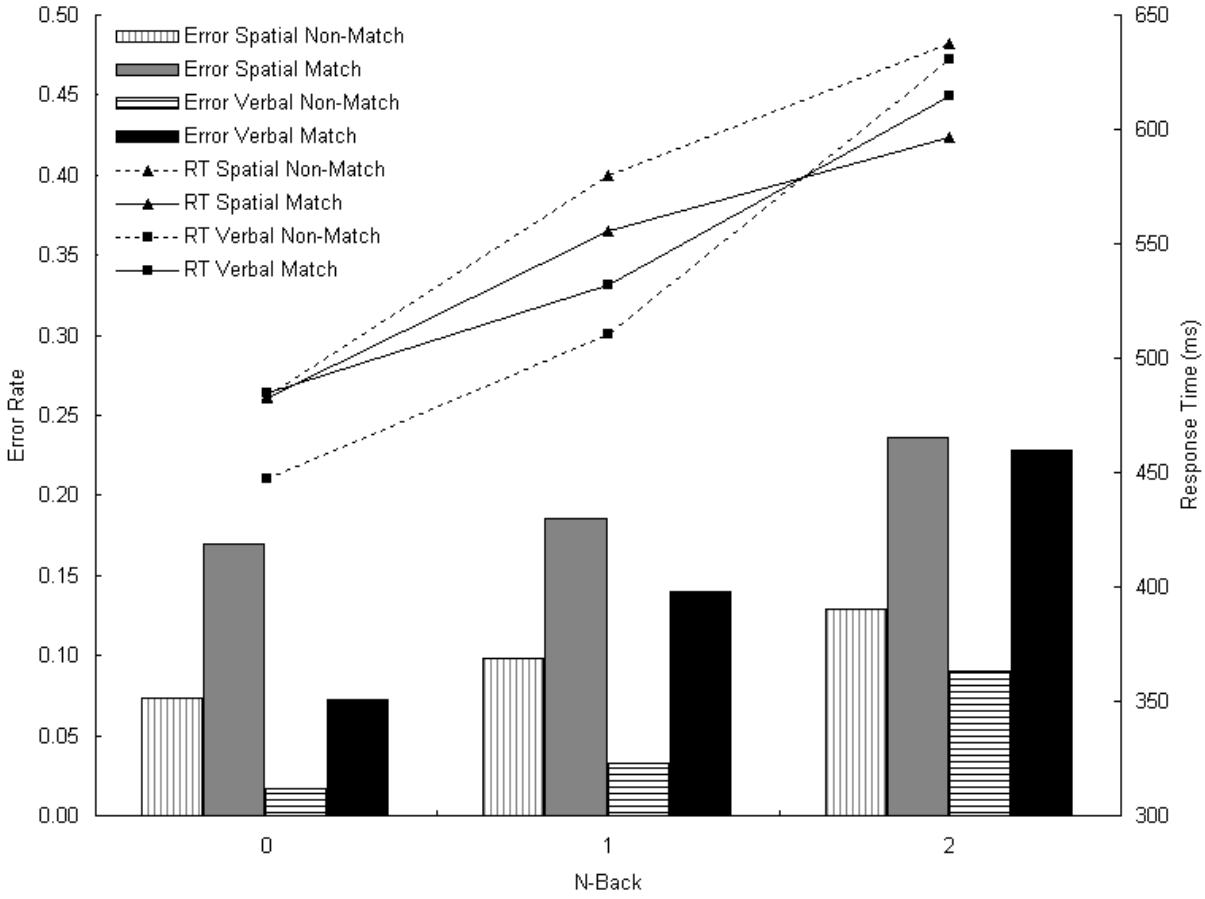

Figure 2-3. *Response time (lines) and error rate (bars) in 0-, 1-, and 2-back conditions, separately for spatial and verbal tasks, and separately for match and non-match trials.*

2.3.1.2. Error rate

Error rate was higher in target stimuli than in non-target ones, as evidenced by a significant Stimulus effect, $F(1, 50) = 114.03$, $p < .001$, higher in spatial tasks than in

verbal tasks, as evidenced by a significant Task effect, $F(1,50) = 8.02$, $p = .007$, and increased pertaining to the memory loads, as evidenced by a significant N-Back effect, $F(2, 100) = 34.15$, $p < .001$. Other main effects or interactions were non-significant in error rate, all $F < 3.13$, all $p > .059$

2.3.2. Electrophysiological data

2.3.2.1. Overall ERPs

The grand mean ERP waveforms, collapsed across the N-back factor, are presented in Figure 2-4. Mean amplitudes under every condition are presented for EPC in Figure 2-5, P2a in Figure 2-6, N2 in Figure 2-7 and P3 in Fig 3-8. Due to the large number of statistics, *F- and p*-values are presented in Table 3-1 rather than in the text.

A main effect of Task was obtained only for EPC: During this early latency window, ERPs elicited in the verbal task were generally more negative than ERPs elicited in the spatial task. In contrast, a main effect of Stimulus – with ERPs elicited by matching stimuli being more positive than ERPs elicited by non-matching stimuli – occurred only in the three subsequent latency windows. This match effect was further modified by a Stimulus × Task interaction, which was found to change with time: In the earlier P2a latency window, the match effect was larger in the spatial

than in the verbal task, particularly at midline and left-hemisphere sites. However, within the later two latency windows (N2 and P3) this relationship reversed, and the match effect became larger in the verbal task, again particularly in the left hemisphere (at midlines sites, the Stimulus × Task interaction was significant only in the P3 latency range). Finally, the match effect was found to increase with increasing n in the N2 latency window, but only for the verbal, not for the spatial task, as evidenced by a significant N-Back × Stimulus × Task interaction.

A main effect of N-Back – with ERP amplitudes becoming increasingly positive with increasing n – was evident at midline sites in all three earlier latency windows (EPC, P2a, and N2), and at lateral sites during the EPC- and N2-latency windows. Initially (i.e., within the EPC latency window), this effect was lateralize d to the right hemisphere. However, an N-Back × Task interaction in the P3 latency range was due to the fact that within this time window, the N-Back effect reversed its direction (i.e., amplitudes were less positive for higher values of N) under verbal task instructions. Furthermore, a three-way interaction of N-Back × Task × Hemisphere was observed in the P2a and N2 latency windows, as the N-Back effect was particularly pronounced in the right hemisphere under spatial task instructions, but in the left hemisphere under verbal task instructions. Finally, N-Back effects were larger for matching than for non-matching stimuli (N-Back × Stimulus interaction),

and this difference was significant in the N2 latency range.

It seems no follow-up analyses were carried out, which makes interpretations of interactions difficult. In particular statements like ‘found to increase with increasing n in the N2 latency window, but only for the verbal, not for the spatial task’ are not warranted without analysis of the effects for the tasks separately.

			EPC			P2a			N2a			P3		
	Effects	df	*F*	*p*		*F*	*p*		*F*	*p*		*F*	*p*	
Non-Midline	Task	(1,50)	7.16	0.010	*	2.85	0.098		3.73	0.059		0.70	0.407	
	Stimulus	(1,50)	0.77	0.385		23.29	0.000	*	20.37	0.000	*	108.03	0.000	*
	Stimulus × Task	(1,50)	0.66	0.422		6.51	0.014	*	2.31	0.135		8.25	0.006	*
	Hemisphere	(1,50)	0.16	0.692		0.11	0.746		0.20	0.659		2.15	0.149	
	Hemisphere × Task	(1,50)	0.66	0.422		0.88	0.354		1.45	0.234		1.70	0.198	
	N-Back	(2,100)	4.16	0.023	*	2.32	0.104		4.28	0.021	*	1.81	0.173	
	N-Back × Task	(2,100)	2.47	0.097		1.00	0.373		0.60	0.534		2.92	0.065	
	Hemisphere × Stimulus	(1,50)	3.89	0.054		0.25	0.620		0.65	0.425		0.07	0.790	
	Hemisphere × Stimulus × Task	(1,50)	0.16	0.688		8.01	0.007	*	7.10	0.010	*	5.79	0.020	*
	Hemisphere × N-Back	(2,100)	5.44	0.006	*	1.14	0.326		1.82	0.168		1.13	0.328	
	Hemisphere × N-Back × Task	(2,100)	1.68	0.193		4.68	0.011	*	3.59	0.031	*	1.76	0.177	
	N-Back × Stimulus	(2,100)	0.75	0.475		1.93	0.150		3.60	0.031	*	1.11	0.333	
	N-Back × Stimulus × Task	(2,100)	1.17	0.315		1.04	0.359		2.67	0.074		1.00	0.372	
	Hemisphere × N-Back × Stimulus	(2,100)	0.62	0.538		2.13	0.126		0.95	0.388		0.92	0.402	
	Stimulus × Hemisphere × N-Back × Task	(2,100)	1.18	0.312		1.60	0.207		0.43	0.655		1.08	0.334	
Midline	Task	(1,50)	8.00	0.007	*	3.10	0.084		1.51	0.225		0.06	0.808	
	Stimulus	(1,50)	0.23	0.635		16.11	0.000	*	91.89	0.000	*	140.86	0.000	*
	Stimulus × Task	(1,50)	0.76	0.387		0.11	0.744		13.53	0.001	*	19.90	0.000	*
	N-Back	(2,100)	6.68	0.003	*	7.92	0.005	*	4.73	0.017	*	2.33	0.111	
	N-Back × Task	(2,100)	2.74	0.076		1.05	0.347		0.99	0.361		3.39	0.045	*
	N-Back × Stimulus	(2,100)	0.16	0.852		1.30	0.283		1.46	0.238		1.93	0.151	
	N-Back × Stimulus × Task	(2,100)	1.11	0.333		0.673	0.513		5.486	0.006	*	1.093	0.339	

Table 2-1. *Omnibus ANOVA of ERP results (Task = verbal versus spatial task; Stimulus = matching versus non-matching stimulus; Hemisphere = left versus right hemisphere; N-Back = 0-back versus 1-back versus 2-back task). Significant effects ($p < .05$) are marked with star.*

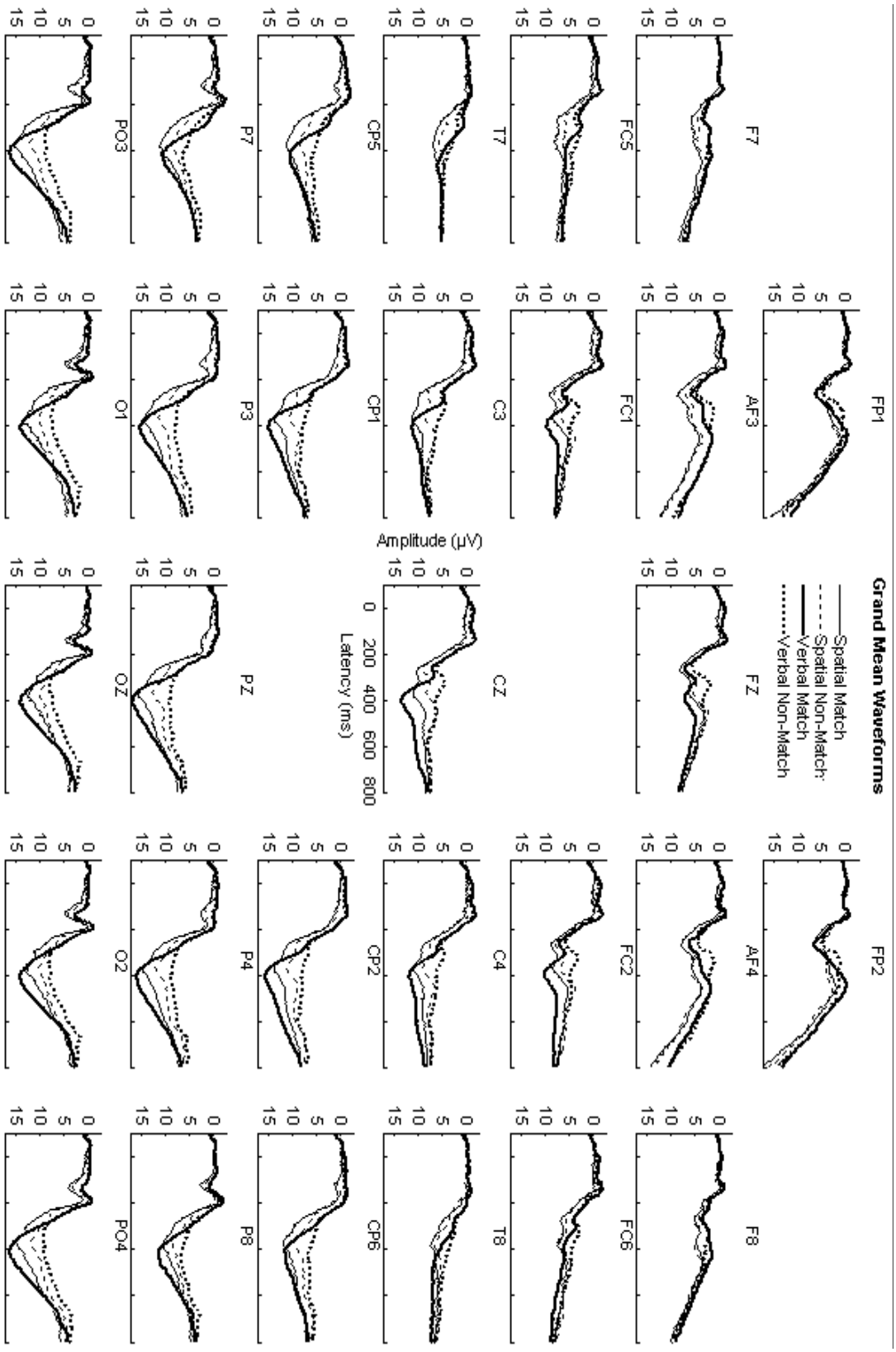

Figure 2-4. *Grand mean ERP waveforms, collapsed across the N-back factor, elicited during for spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items are indicated. Dashed lines indicate ERPs elicited by non-matching items.*

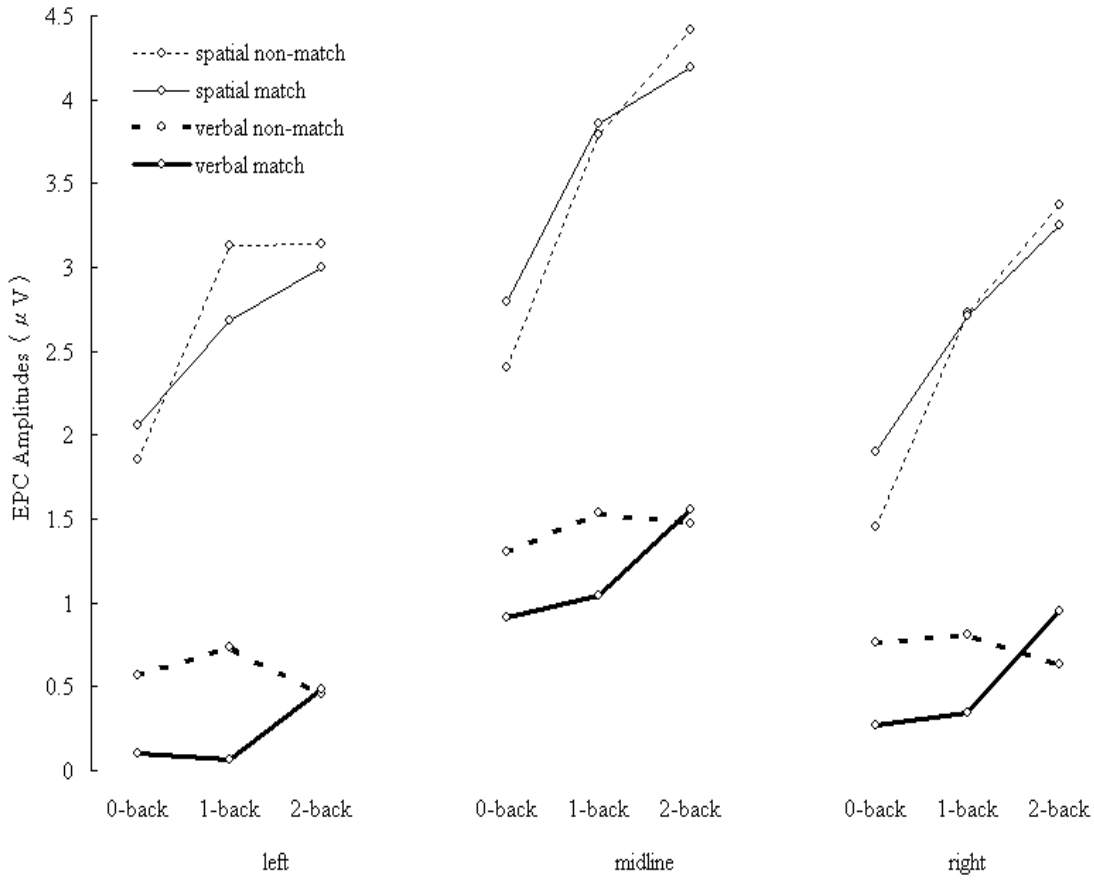

Figure 2-5. *EPC amplitudes elicited during spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

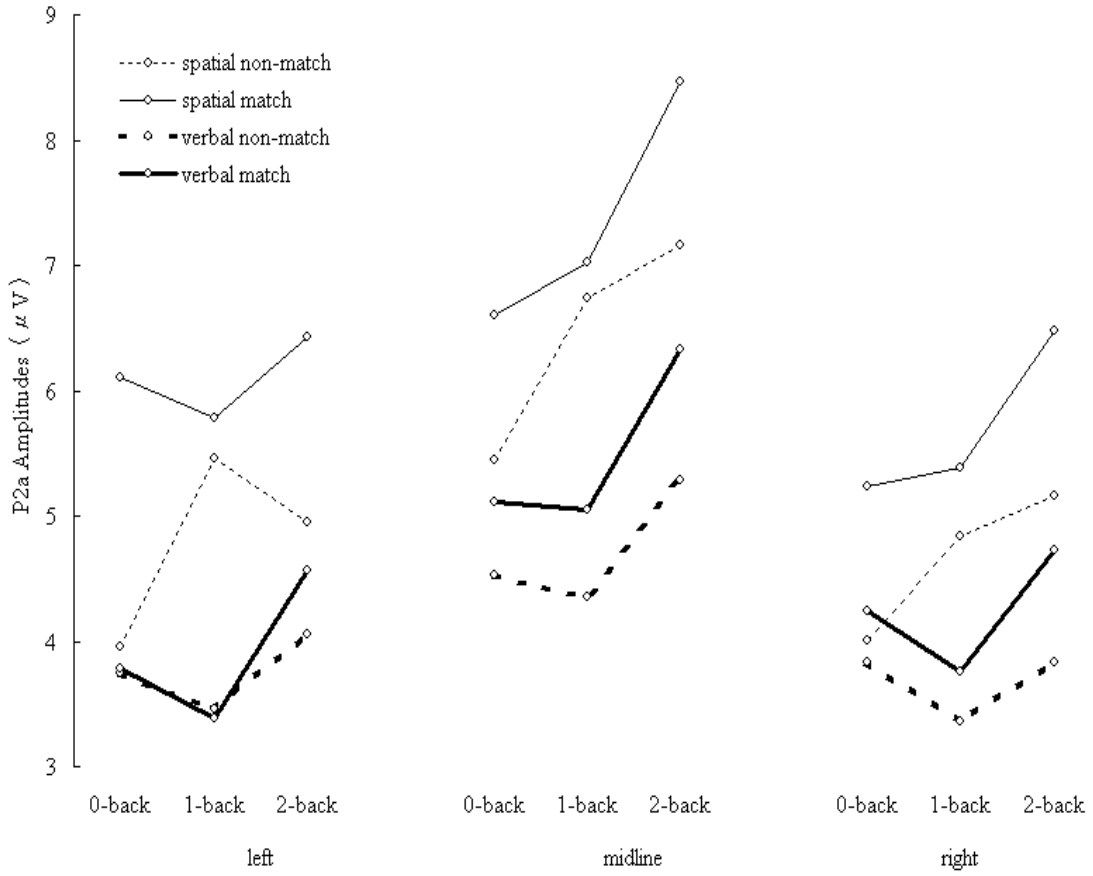

Figure 2-6. *P2a amplitudes elicited during spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

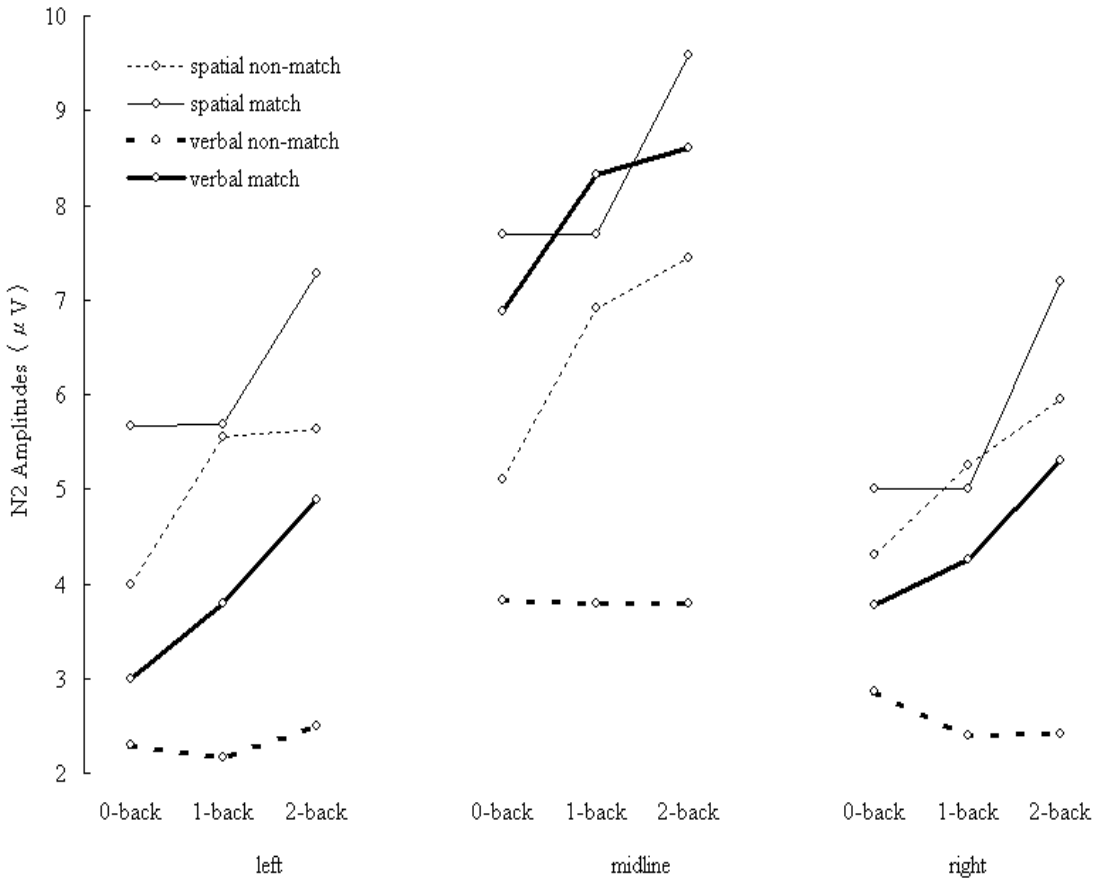

Figure 2-7. *N2 amplitudes elicited during spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

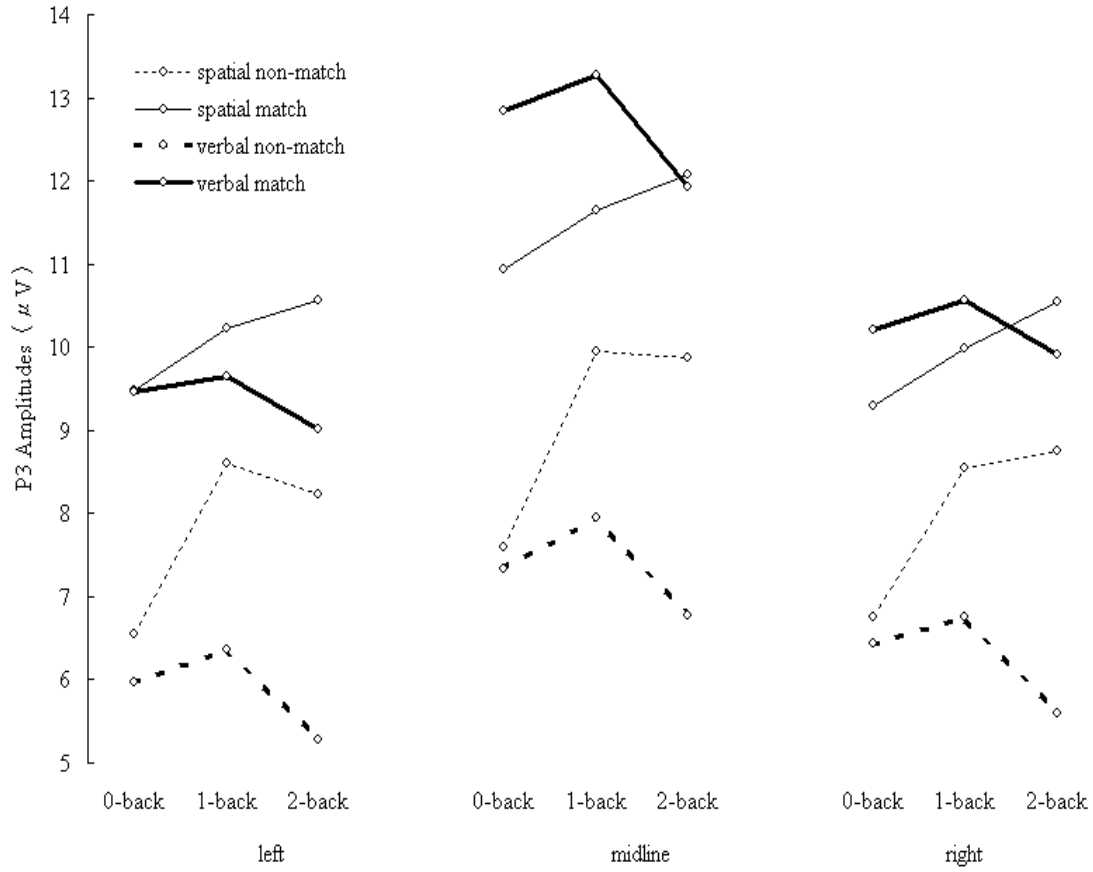

Figure 2-8. *P3 amplitudes elicited during spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

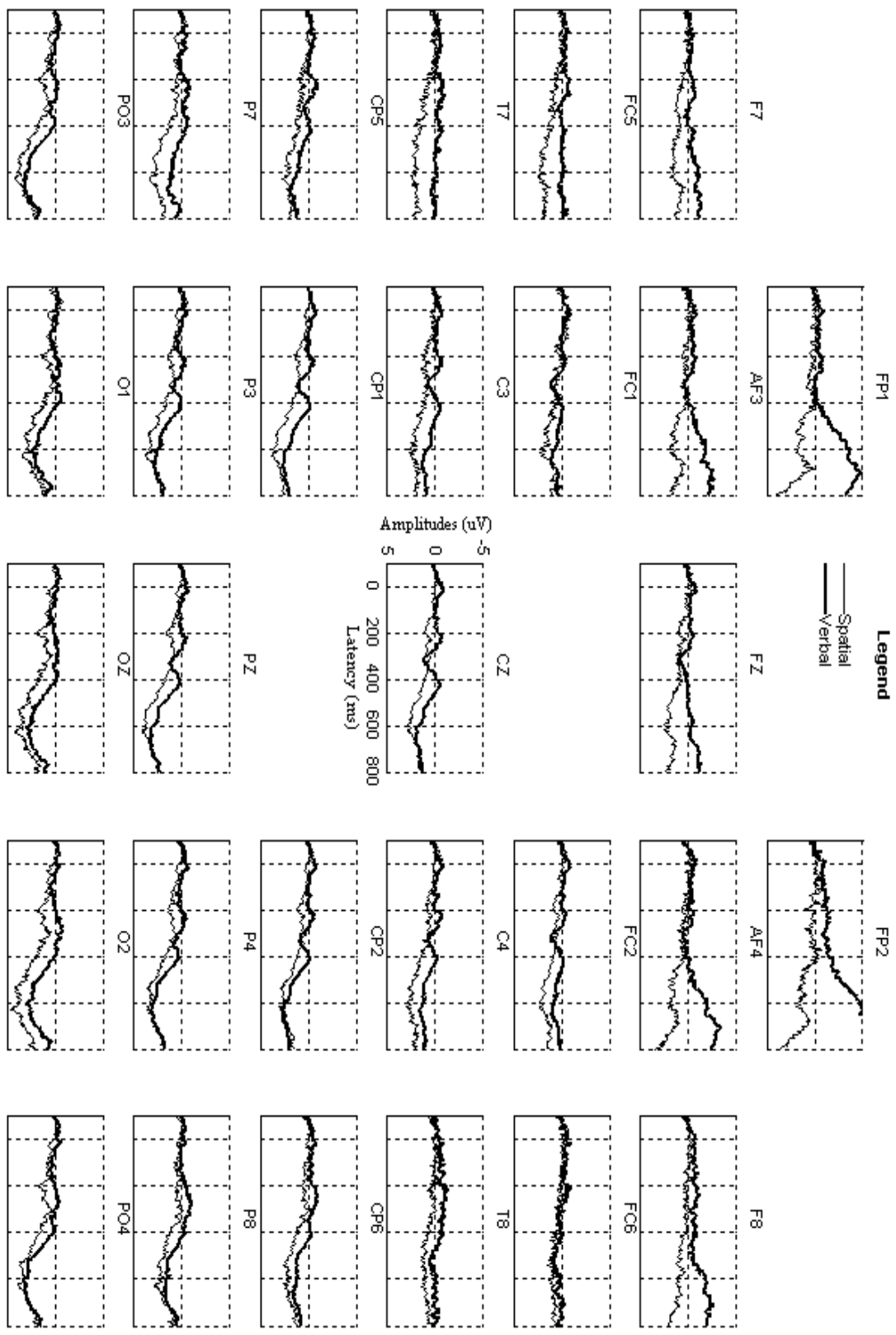

Figure 2-9. *Replacement effects (1-back minus 0-back difference waveforms), separately for spatial (thin line) and verbal (think line) task instructions, collapsed across stimulus types (match and non-match).*

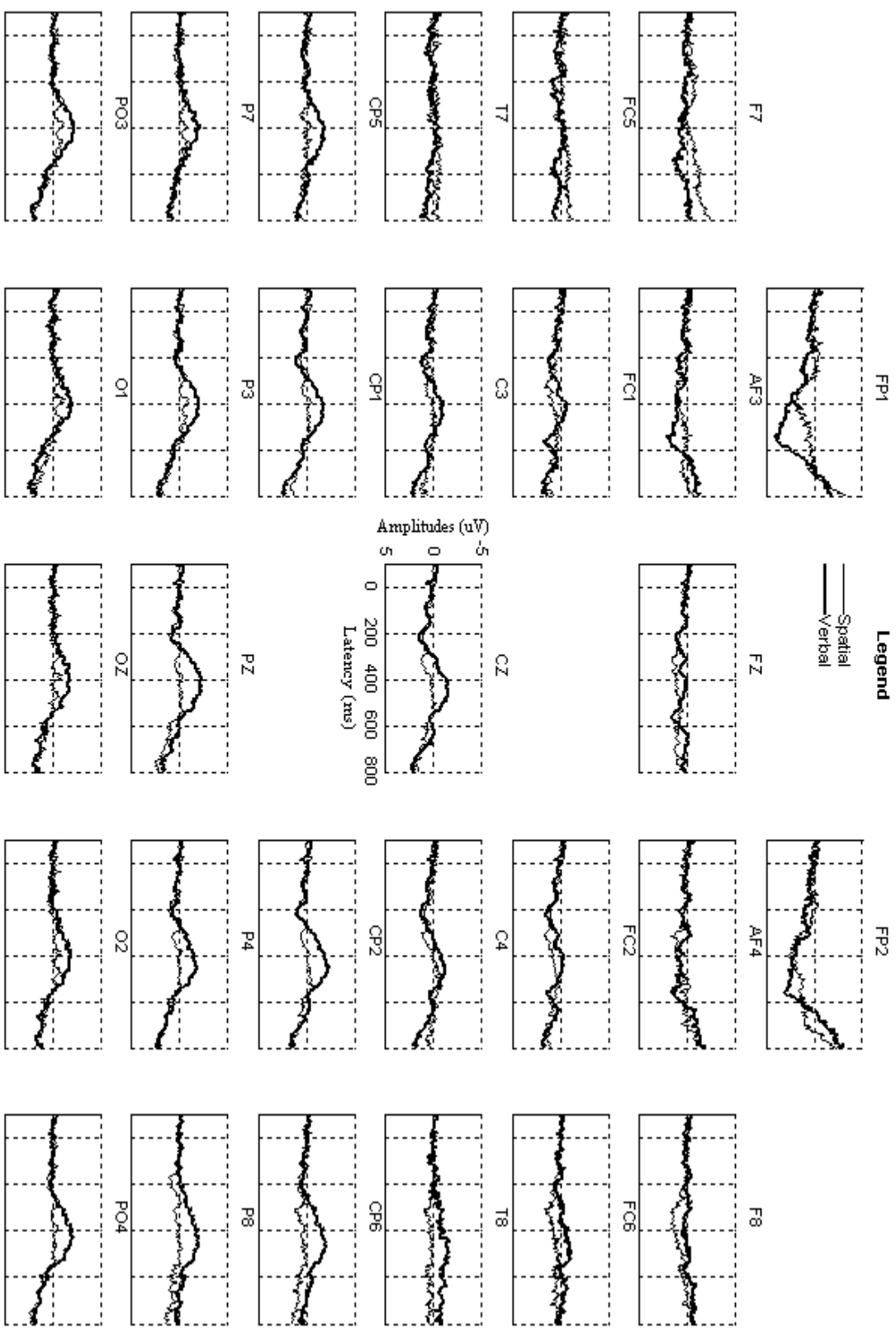

Figure 2-10. *Shift effects (2-back minus 1-back difference waveforms), separately for spatial (thin line) and verbal (think line) task instructions, collapsed across stimulus types (match and non-match).*

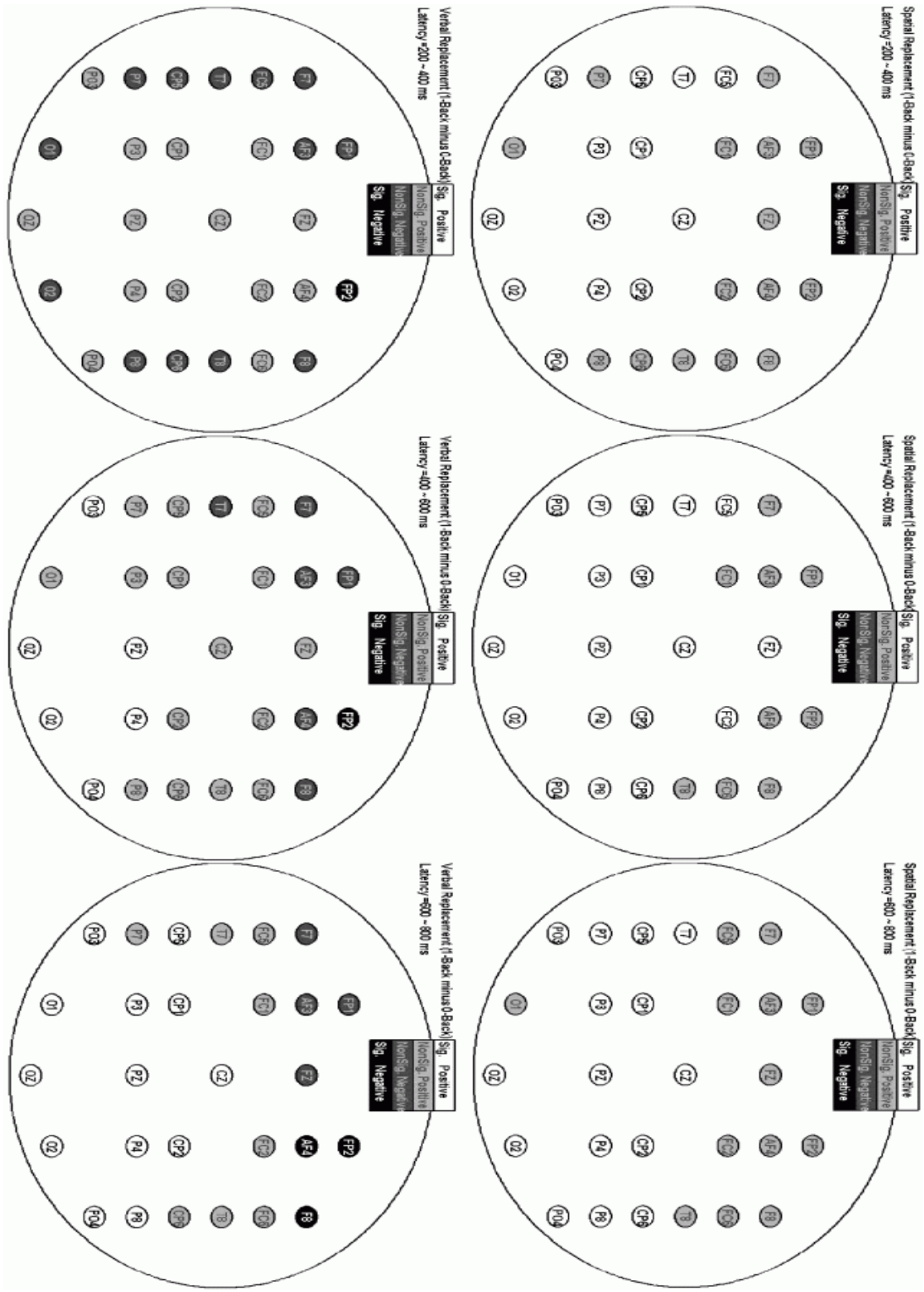

Figure 2-11. *Replacement effects (1-back minus 0-back difference) in the three successive latency windows (200-400 ms, 400-600 ms, 600-800 ms), separately for spatial and verbal task instructions, by t-Statistical Maps. White: significant positive; light grey: non-significant positive; dark grey: non-significant negative; black: significant negative.*

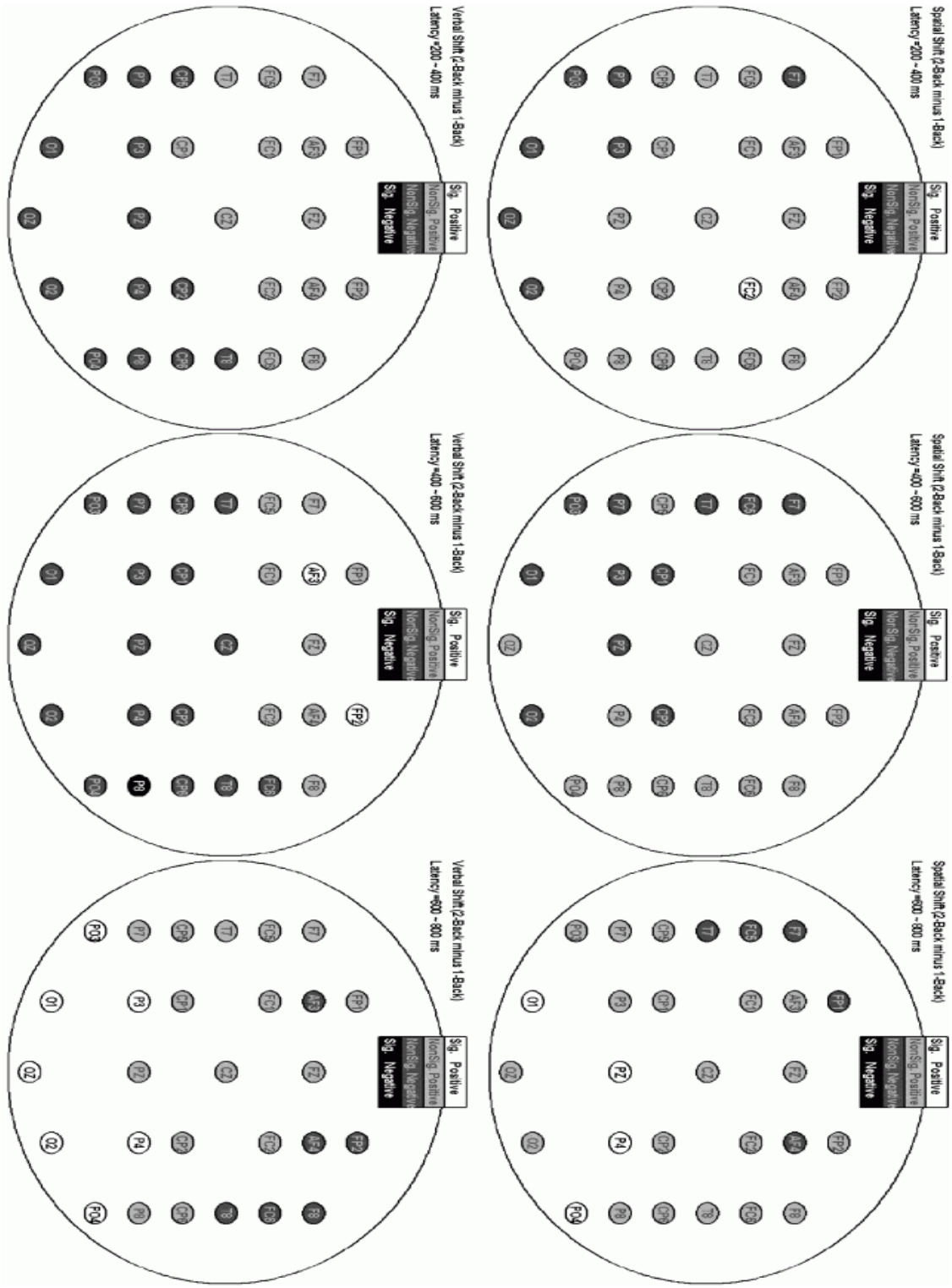

Figure 2-12. *Shift effects (2-back minus 1-back difference) in the three successive latency windows (200-400 ms, 400-600 ms, 600-800 ms), separately for spatial and verbal task instructions, by t-Statistical Maps. White: significant positive; light grey: non-significant positive; dark grey: non-significant negative; black: significant negative.*

2.3.2.2. Replacement and shift effects

The following analyses were conducted to investigate sub-processes of the N-back task, and were carried out on the 1-back minus 0-back difference waveform ('replacement effect') and on the 2-back minus 1-back difference waveform ('shift effects'). ERP difference waveforms are presented in Figure 2-9 and Figure 2-10. *t*-statistical maps (Figure 2-11 and Figure 2-12) depict the direction of amplitude differences (positive versus negative) within the three analysis windows, and highlights electrodes where these differences were statistically significant (i.e., *p*s < .05, uncorrected).

Under spatial task instructions, replacement was accompanied by a general positive shift, which was significant at most of central and posterior sites in all three latency windows. Under verbal task instructions, in contrast, replacement was characterized by an anterior negativity and posterior positivity. This pattern developed over time, with mostly non-significant shifts in the earlier time-windows, and significant right-frontal negative and central-posterior positive shifts in the 600 – 800 ms window.

2.3.2.3. Omnibus ANOVA of replacement effects

From ANOVA, no significant replacement effects were obtained in the earliest time

window (200-400 ms), all $F < 3.23$, all $p > .078$. In the mid- and the late-latency window (400-600 and 600-800 ms), replacement-amplitudes increased from anterior to posterior sites as evidenced by ACP effects (see Figure 2-12), $F(2,100) = 10.26$, $p = .001$, and $F(2,100) = 18.00$, $p < .001$, respectively. In the late window, an ACP × Task interaction showed that this increase was far steeper under verbal task instructions (where amplitudes were even substantially negative at anterior sites) than under spatial task instructions, $F(2,100) = 5.37$, $p = .018$. Generally, the replacement effect was larger for non-matching than for matching stimuli in the left hemisphere, whereas no such difference was observed in the right hemisphere. However, this interaction became significant only in the last latency window, as evidenced by a Stimulus × Hemisphere interaction, $F(1,50) = 4.86$, $p = .032$. No other significant main effects or interactions were obtained in the replacement analysis in 400-800 ms. Other *F*s were lesser than 3.16 and other *p*s were greater than .071.

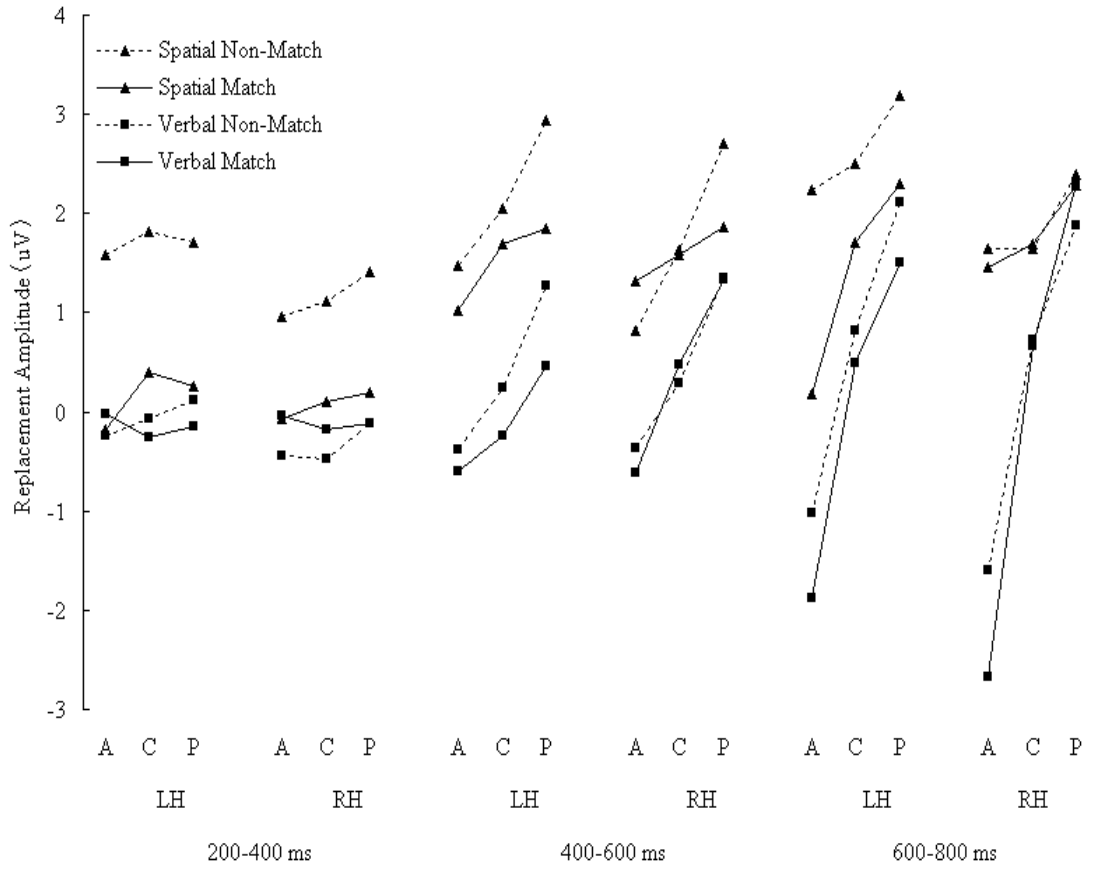

Figure 2-13. *Replacement amplitudes elicited during spatial (triangle) and verbal (square) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items. A: Anterior; C: Central; P: Posterior; LH: Left Hemisphere; RH: Right Hemisphere.*

2.3.2.4. Omnibus ANOVA of shift effects

Under both task instructions, shift effects were characterized by an anterior positivity and posterior negativity in the early and the mid-latency time window, although these effects were significant only at few individual electrode sites (see Figure 2-8). During the last latency window, this pattern reversed, as a negative shift developed at anterior sites and a positive shift at posterior sites.

A significant Stimulus effect was found in the early latency window, where shift effects were larger for matching than for non-matching stimuli, $F(1,50) = 6.18$, $p = .016$. ACP effects were significant in the early- and the mid-latency window (200-400 and 400-600 ms), where shift-amplitudes decreased from anterior to posterior sites (see Figure 2-14), $F(2,100) = 5.50$, $p = .016$, and $F(2,100) = 5.78$, $p = .015$, respectively. In all three latency windows, shift effects were larger in the left than in the right hemisphere under verbal task instructions, and were larger in the right than in the left hemisphere under spatial task instructions, as evidenced by significant Task × Hemisphere interactions, $F(1,50) = 7.17$, $p = .010$, $F(1,50) = 8.64$, $p = .005$, and $F(1,50) = 4.03$, $p = .050$ for early-, mid- and late-latency windows, respectively. In addition to lateralization to task instructions, match-specific lateralization was also evidenced by significant Stimulus × Hemisphere interactions in the mid- and late-latency windows, where shift effects were larger in the left than in the right hemisphere for matching stimuli, and larger in the right hemisphere than in the left for non-matching stimuli, $F(1,50) = 6.41$, $p = .015$, and $F(1,50) = 12.4$, $p = .001$, respectively. These interactions were further scrutinized by a three-way Task × Stimulus × ACP interaction: In anterior and central electrodes, shift-amplitudes in the time window 400 - 600 ms were more positive-going in response to the matching stimuli than to the non-matching ones under verbal task instructions, but more

positive-going in response to the non-matching stimuli than to the matching ones under spatial task instructions. In posterior electrodes, those amplitudes were more positive-going under spatial task instructions than under verbal task instructions in response to whatever stimulus types, $F(2,100) = 4.25$, $p = .036$. No other significant main effects or interactions were obtained in the shift analysis, all Fs < 3.39, all ps > .0.071.

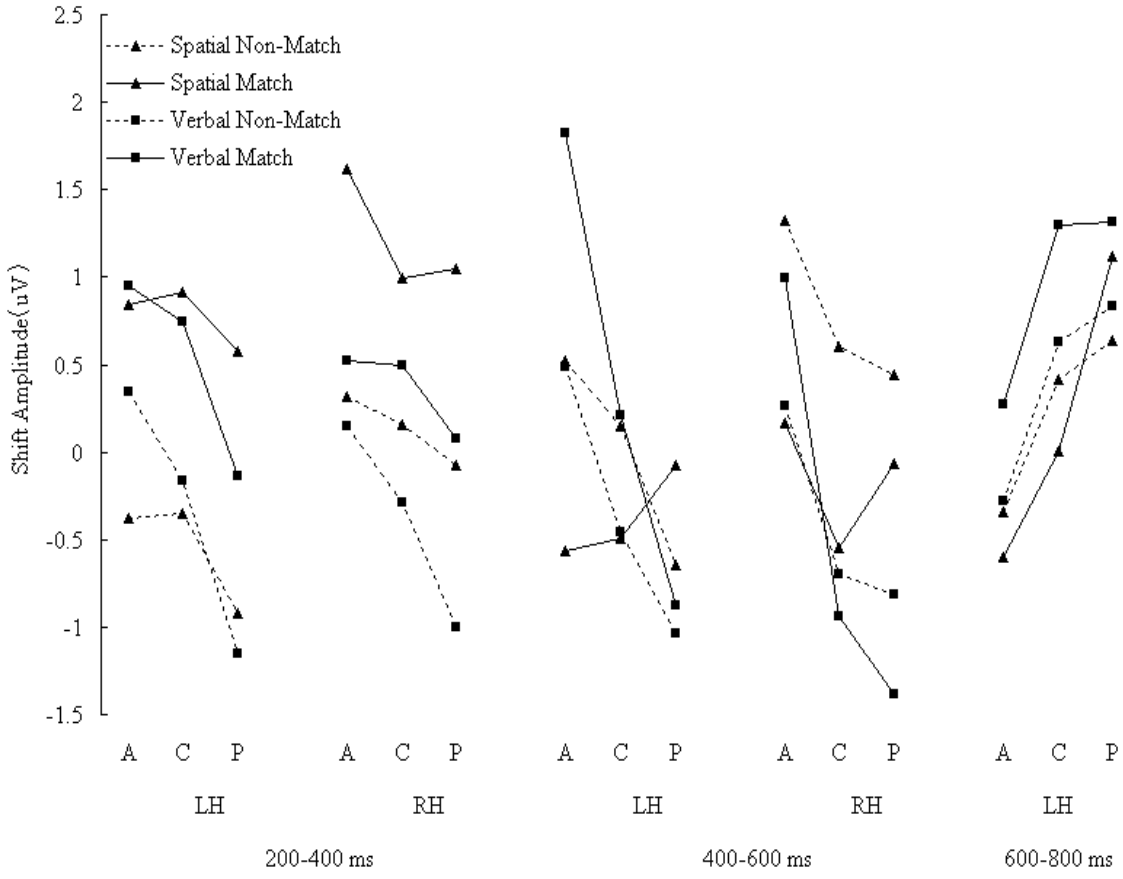

Figure 2-14. *Shift amplitudes elicited during spatial (triangle) and verbal (square) tasks. Dashed lines indicate ERPs elicited by matching items. Solid lines indicate ERPs elicited by non-matching items. A: Anterior; C: Central; P: Posterior; LH: Left Hemisphere; RH: Right Hemisphere.*

2.4. Discussion

The experiment one investigated the electrophysiological correlates of verbal and spatial WM in the N-back task with varying working memory load. In the following, I will first discuss the overall ERP effects of task instruction and working memory load. Subsequently, we will consider the ERP evidence for distinct sub-processes in the N-back task and their possible differences depending on task instructions.

2.4.1. Overall ERPs

The only main effect of task instructions was obtained in the EPC-latency range (150 – 250 ms after stimulus onset) at posterior electrode sites, where mean ERP amplitudes were more negative under verbal than under spatial instructions. There were no main effects of task instruction in any of the subsequent time windows, nor was there any evidence for differential lateralization of verbal and spatial tasks. These results contrast with earlier findings of task-specific lateralization even when stimulus material is held constant (Smith & Jonides, 1997), and appear to be more in line with the assumption that WM is a unitary mechanism which is not subdivided into modality-specific subsystems (e.g., Ross & Segalowitz, 2000).

However, this picture was complicated by the analysis of matching versus

non-matching stimuli. As expected, infrequent matching stimuli elicited more positive-going ERPs than frequent non-matching stimuli from approximately 200 ms post-stimulus onwards at anterior and particularly at centro-parietal sites, in line with effects elicited by infrequent stimuli in oddball paradigms (e.g., Bennington & Polich, 1999). Unexpectedly, though, this 'matching' effect was initially larger under spatial task instructions at anterior sites in the P2a-latency window (in fact, it was virtually absent under verbal task instructions in this latency window). Subsequently, it became larger under verbal than under spatial task instructions both at anterior and at central-posterior sites in the N2- and P3-latency windows (see McEvoy, Smith, & Gevins, 1998a, Figure 3, for a similar pattern). Taken together, this pattern can be interpreted as indicating that relative to a negative match (rejection), a positive match was faster and required less effort under spatial than under verbal task instructions, and inline with the previously reported finding (e.g., Rueda, Posner, Rothbart, & Davis-Stober, 2004; Ullsperger, Metz, & Gille, 1988). This interpretation also fits with the match/non-match effects observed for RT, which where larger under verbal task instructions, and smaller (in fact, reversed) under spatial task instructions.

Unlike McEvoy *et al.* (1998a), who observed a left-lateralize d P3 component, the present study did not find any general amplitude differences between hemispheres. Match effects, however, were found to be larger in the left than in the right

hemisphere, both under spatial task instructions (P2a latency window at anterior sites) and under verbal task instructions (subsequent latency windows at anterior and central-posterior sites). Given that in the McEvoy et al.'s study, participants always responded with the right hand, whereas in the present experiment, match- and nonmatch-responses were assigned to left- and right-hand responses, counterbalanced across participants, one might argue that the former effect is influenced by lateralized motor processes, whereas the present effect indicates that the left hemisphere was more strongly involved in the match/non-match decision process than the right hemisphere regardless of task instructions. This might be taken as evidence that matching is a modality-unspecific WM process mediated by left-hemispheric structures. However, this is not the only possible interpretation. In particular, one might speculate that the left-lateralize d match effect indicates that participants employed verbal encoding strategies both under verbal and under spatial task instructions. It is well known, for example from the so-called Stroop-effect, that words will be read and understood even if such semantic processing is not only not helpful, but in fact interferes with task performance (for a review, see, e.g., (MacLeod, 1991). Therefore, it seems safe to assume that participants in the spatial task conditions did process the stimulus words semantically – thereby engaging left-hemispheric structures – even though word meaning was not task relevant.

Additionally, the possibility can not be ruled out that under spatial task instructions, participants encoded the stimulus location verbally ("top," "bottom," "top left," etc.), which also would favor left-hemisphere processing.

Of particular interest is the finding that in the N2 latency window, the anterior match effect increased with increasing N under verbal, but not under spatial task instructions. As can be seen from Figure 2-7, this was due to the fact that whereas in all other conditions, amplitudes increased with increasing N, N2-amplitudes triggered by verbal non-matching stimuli remained constant. These data suggest that the rejection of a non-matching stimulus word under verbal task instructions is not a load-sensitive process, whereas rejecting a non-matching stimulus under spatial task instruction, and recognition of a matching stimulus under either instruction, are load-sensitive processes. However, the behavioral data (see Figure 2-3) do not confirm this conclusion, as RT and error rate for verbal non-matching stimuli increased with increasing N at least as much as in the other conditions. Therefore, it has to be concluded that the anterior N2 reflects a specific sub-process which does not contribute directly to response time, and which is different in verbal and spatial tasks.

N2 is selective sensitive to the match sub-process. As mentioned, N2 is present for a negative matching process. There are objects in spatial tasks – location-matching or non-matching. However, there are only objects in verbal matching tasks but no

objects in verbal non-matching tasks. Therefore, it is reasonable that N2 is flat in a verbal non-match process.

Overall, ERP amplitudes increased with increasing N in the earlier three latency windows (particularly for matching items), and decreased with increasing N in the P3 latency window. The former effect was particularly pronounced in the right hemisphere under spatial task instructions, whereas it was of approximately equal size in both hemispheres under verbal task instructions. Furthermore, the reduced P3 amplitude with increasing N replicates McEvoy et al.'s (1998) finding, with the notable exception that here, it was observed only under verbal, but not under spatial task instructions. Overall, this pattern of results fits with the assumption that spatial features of the stimulus material are processes whether or not they are response relevant (Meegan & Honsberger, 2005); see also (Ravizza, Behrmann, & Fiez, 2005).

Taken together, these results indicate systematic differences between WM processes concerning spatial and verbal aspects of identical stimulus displays, even under conditions where processing of spatial features under verbal instructions, and of verbal content under spatial instructions, seems likely. However, these differences are considerably more subtle than general lateralization of activity to the right under spatial and to the left under verbal task instructions (Stephan *et al.*, 2003), and in particular suggest that brain is differentially mobilized by task instructions.

2.4.2. Sub-processes of the N-back task

The electrophysiological results of this experiment suggest that the shift sub-process was left-lateralized in the verbal version, and right-lateralized in the spatial version of the task. This pattern persisted across all the three latency windows that were examined, whereas the corresponding effects for the replacement sub-process were not statistically significant at any latency. Since the stimuli in the present task were identical in the spatial and verbal versions of the task, with the aspect of interest indicated conceptually (i.e., by instruction alone), the above result is consistent with the hypothesis that the replacement sub-process is mostly data-driven whereas the shift sub-process is more conceptually controlled (and therefore more affected by manipulations in this conceptually driven version of the N-back task). Furthermore, amplitudes in the replacement sub-process increased but amplitudes in the shift sub-process decreased from anterior to posterior sites. This pattern was found in the 400-600 ms and 600-800 ms time windows for replacement, and in the 200-400 ms and 400-600 ms time windows for shift. This finding also supports our initial hypothesis that the replacement sub-process primarily engages perceptual processes in the posterior area whereas shift involves executive processes in the frontal area.

The behavioral results showed the expected increase in RT with increasing N,

with an accompanying decrease in accuracy. Similarly, detection of match stimuli was less accurate than non-match ones, and there was an indication that the spatial version of the task was more error-prone, and therefore possibly the harder of the two. In addition, RT to non-match stimuli was greater than to match stimuli in the spatial task, but the opposite was true in the verbal task. Moreover, as N increased, non-match stimuli took longer to identify than match stimuli in the same condition.

This experiment also found electrophysiological distinctions in the processing of match and non-match stimuli during the N-back task. In the shift sub-process in particular, amplitudes in the match condition were greater than in the non-match condition in the earliest examined time window (200-400 ms). Thereafter, in the 400-600 ms and 600-800 ms time windows, the match condition was left-lateralized whereas the non-match condition was right-lateralized. Also, in the 400-600 ms time window, anterior and central amplitudes were greater for match than for non-match stimuli in the verbal task, but it was the opposite in the spatial task. Taken together, these electrophysiological and behavioral results suggest that the view of matching as a constant-load, early-latency subtask of the N-back task (Watter *et al.*, 2001) may be too simplistic. Our logical analysis (Figure 2-1) followed this view in assuming that matching occurs as an encapsulated first component of an N-back trial. As such, our task analysis provides no means of explaining either the observed changes in RT to

match and non-match stimuli as N increased, or the match-based lateralization effects in the shift sub-process in later time windows. We revisit this issue in the second experiment and present our conjectures the general discussion.

On a final cautionary note, it should be emphasized that of course the 1-back minus 0-back waveforms do not exclusively reflect replacement effects, and the 2-back minus 1-back waveforms not exclusively shift effects. Although the different sub-processes under the N-back task will have contributed to these difference waveforms, any non-specific, load-sensitive processes will have influenced them as well. At present, it is not possible to clearly delineate the contribution of different sub-processes, as the experiment necessarily allowed only a limited number of manipulations. Future research might investigate these issues further, by comparing, for example, ERPs elicited by verbalizable versus non-verbalizable spatial stimuli, and by spatially distributed versus non-distributed verbal stimuli, in order to tease apart the influence of material-specific (bottom-up) and strategic (top-down) influences on WM processes.

Chapter 3. Experiment 2: Interference from the Irrelevant Domain in N-Back Tasks

3.1. Introduction

In order to reduce as many irrelevant factors as possible, Experiment 1 applied identical stimuli in different domains as different tasks to eliminate influences from the perceptual differences and allowed "direct" comparison between tasks. However, a new factor – the cross-domain interference – is inevitably introduced. Cross-domain interference refers to interference from the stimulus feature that is not relevant, but may nevertheless be extracted. The irrelevant stimulus feature could interfere with the matching process of the relevant feature, depending on whether the irrelevant feature matching that of the item kept in working memory. Participants are assumed to perform top-down control to process the relevant domain and ignore the irrelevant domain in sub-processes of N-back tasks. The key point is whether selective attention excludes cross-domain influence from the early latency or let the influence sustain until the end of information processing.

Based on behavioral studies using letter and position N-back tasks, (Meegan & Honsberger, 2005) concluded that irrespective of the actual stimulus material or task demands, N-back task performance always involves both spatial and verbal processing. This conclusion fits with neuroimaging results (Smith & Jonides, 1997). Thus, it is reasonable to assume that participants process both domains but attempt to actively exclude the irrelevant domain later. In contrast, early effects of selective

attention have been demonstrated in a number of event-related potential (ERP) studies of WM (Awh *et al.*, 1998; Berti & Schroeger, 2001; Wolach & Pratt, 2001). Domain-specific distracter effects (Lange, 2005; Lawrence, Myerson, & Abrams, 2004), where auditory distracters only affected verbal memory and visual-spatial distracters only affected spatial memory, were reported. However, the experimental design in such studies frequently aims to maximize the distinctiveness of spatial and verbal WM tasks, whereas under normal conditions, stimuli and events in the environment frequently belong to different domains simultaneously. When such multi-modal stimuli are employed, effects tend to be somewhat less clear-cut (Lange, 2005), and might even indicate cross-modal or supra-modal distracter effects (Logie, Zucco, & Baddeley, 1990).

As yet, the mechanisms underlying such effects are unclear. Experiment 2 aimed to close this gap by investigating the temporal course of cross-domain interference with ERP, which has high temporal resolution. Words are presented at different screen locations, and participants must either respond to stimulus identity (verbal task) or stimulus position (spatial task). Consequently, stimulus features can match the features of the reference stimulus simultaneously in the task-relevant and the task-irrelevant domain. I hypothesized that stimuli with different match-attributes in different domains (for example, non-match in the task-relevant

domain but match in the task-irrelevant domain) will cause cross-domain interference, thus the ERP pattern are expected different from the pattern elicited by stimuli with the same match-attribute in different domains. This hypothesis can be confirmed by ERP patterns in replacement and shift sub-processes (represented by 1-back minus 0-back and 2-back minus 1-back difference waveforms) and from early to late latency windows.

3.2. Methods

3.2.1. Participants

Twelve paid volunteers (seven female) ranging in age from nineteen to fifty (mean twenty-six) years participated in the experiment. All participants were Caucasians and English native-speakers. According to self-report, all had normal or corrected-to-normal vision, and half of the participants were right-handed.

3.2.2. Stimulus and apparatus

Stimulus presentation and data acquisition were managed by C-programs and running under MS-DOS. Behavioral and affect data were stored on the hard disc driver.

Stimuli were twenty English words with similar frequency and length. Words

were presented in white on black on a 17" computer monitor, at one out of eight circularly arranged positions 4° from the screen centre. Words had a height of approximately 0.8° visual angle, and the width ranged from 3.2° to 6.4° (mean: 5°).

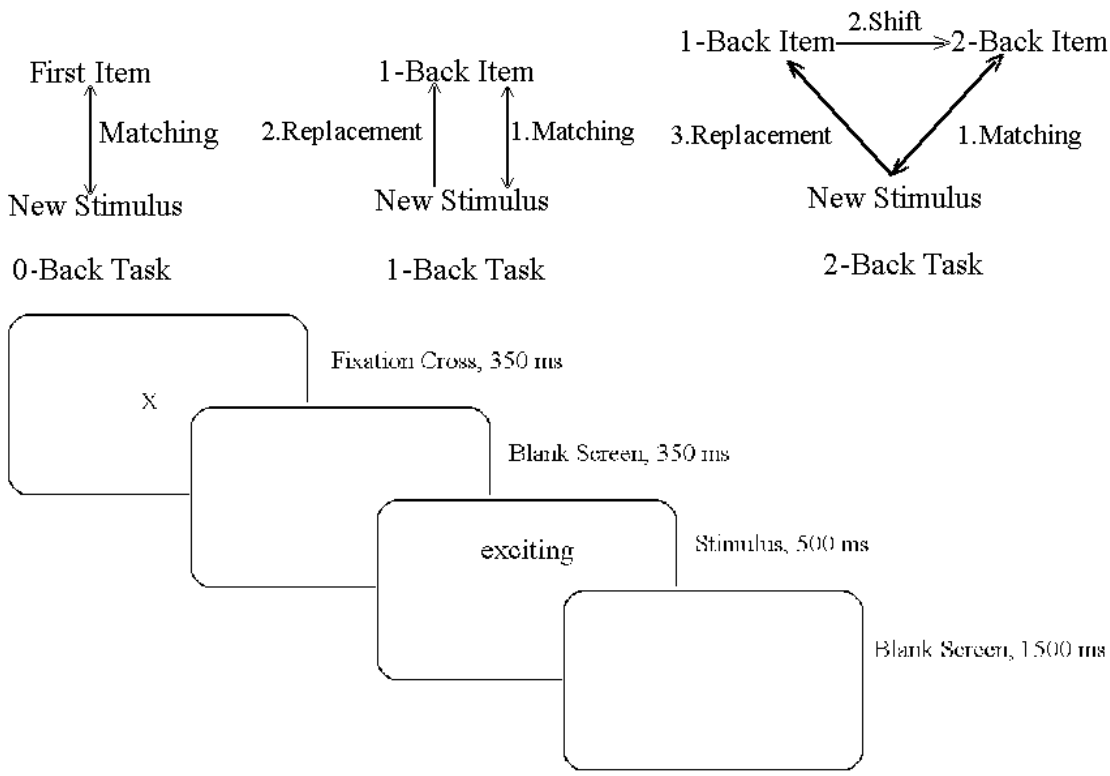

Figure 3-1. *N-back tasks. The upper illustrates logical analyses of N-back tasks. The lower shows trial structure during testing.*

3.2.3. Procedure

Participants were seated in an armchair in front of a computer screen at distance of approximately 60 cm. They were told to keep a comfortable posture, and to avoid eye movements and eye blinks during experimental trials.

Participants completed the first half of the experiment, comprising six blocks of N-back tasks, followed by a break, during which participants were encouraged to leave the experimental room. They then completed the second half of the experiment.

Each experimental half consisted of two 0-back blocks, two 1-back blocks, and two 2-back blocks in sequence. In the first half, each pair of blocks was preceded by a corresponding practice block, to familiarize participants with the changing task requirements. In the second half, no practice blocks were administered. Experimental blocks consisted of sixty-four trials (thirty-two match trials and thirty-two non-match trials). Each trial began with the presentation of a fixation cross in the centre of a screen for 350 ms, followed by 350 ms of a blank screen. Then a stimulus word was shown for 500 ms at one of the eight predefined screen locations. This was followed by another blank screen for 1500 ms (see Figure 3-1). In all blocks, identity and location of each stimulus were determined pseudo-randomly, to achieve an approximately even distribution of targets and an approximately equal distribution of identities and locations. Practice blocks were constructed in the same way, but contained only twenty trials and provided additional feedback (the words “correct” or “wrong” presented in the centre of the screen) immediately after the participant’s response. Data from practice blocks was not

saved.

In the 0-back task, participants indicated whether or not each stimulus matched the first one of the block. For the more demanding levels of the N-back task, participants had to match the current stimulus with the previous stimulus (1-back task) or the stimulus before the previous one (2-back task). Participants pressed a "yes" key for a match (match stimulus) and a "no" key or a mismatch (non-match stimulus). Keys were "\"and "/" keys of a computer keyboard, which had to be pressed with the left and right index finger, respectively. Participants were asked to respond as quickly and accurately as possible, and assignment of keys to "yes" and "no" response was counterbalanced across participants.

Two different versions of the N-back task were employed, and participants were assigned randomly to either of these. In the *verbal version*, the task-relevant feature (RF) of the stimulus words was their identity, whereas their location was irrelevant. In the *spatial version*, the location on the screen was task-relevant, whereas the identity was irrelevant. Note that verbal and spatial versions of the experiment differed only with respect to the instruction given to the participants, and where identical in all other respects. The frequency of match stimuli in either relevant or irrelevant domains was controlled as 50%. The task-irrelevant feature (IF) of the stimulus was compared with the relevant feature, and was marked as IF=Same (IS,

same as the RF) and IF=Different (ID, different from the RF).

3.2.4. Acquisition

Using a BioSemi Active-Two amplifier system, continuous EEG recordings were made with Ag / AgCl electrodes, mounted on a nylon cap, from 32 locations of the international 10–20 system (midline: FZ, CZ, PZ,OZ; left: Fp1, AF3, F7, F3, FC1, FC5, T7, C3, CP1, CP5, P7, P3b, PO3, O1; and corresponding right channels). Sampling rate was 256 Hz. EEG signals were off-line filtered using a 0.01 Hz high pass and a 30 Hz low pass filter, and were re-referenced to linked earlobes.

3.2.5. Pre-processing

Further analysis was conducted using EEGLAB 4.43[14] under the platform of MATLAB 6.1. EEGs were averaged off-line for epochs of 900 ms, starting 100 ms prior to stimulus onset, and ending 800 ms afterwards. Trials containing saccadic eye movement or eye blinks (indicated by amplitudes beyond 3 SD in single channel and 1.5 SD in all channels), and trials where participants gave an incorrect response, were excluded from analysis. EEGs on correct-response trials were averaged for each condition separately, relative to a 100-ms pre-stimulus baseline. Thus for each participant, 12 ERP waveforms were constructed: RF (match / non-match) × IF (IS /

ID) × N-Back (0 / 1 / 2).

3.2.6. Behavioral data analysis

Behavioral data were response time (RT) on correct-response trials and error rate. They were analyzed using a repeated-measure analysis of variance (ANOVA) with the between-subject factor Task (spatial / verbal) and the within-subject factors RF, IF and N-Back.

3.2.7. Electrophysiological data analysis

Latency windows 200-400, 400-600 and 600-800 ms in replacement (1-back minus 0-back) and shift (2-back minus 1-back) processes were selected for analysis. ERP amplitudes, which were defined as mean difference amplitudes within each time window in each electrode, and analyzed separately using *t*-tests for the difference between IS and ID, namely distractedness effects. ERP amplitudes were also tested separately using *t*-tests for the difference from zero baselines. After, *t*-significance probability mapping was performed for presentation of pattern difference between IS and ID. Repeated-measure analyses of variance (ANOVA) were applied for the electrodes F7, AF3, CP5, CP1, P7, P3 and corresponding right channels with the between-subject factor Task (Spatial / Verbal) and the within-subject factors ACP

(anterior / central / posterior), IF (IS / ID) and Hemisphere (Left / Right).

An α-level of .05 was applied for all statistical analyses. Greenhouse-Geisser corrections were applied and corrected *p*-values were reported where appropriate.

3.3. Results

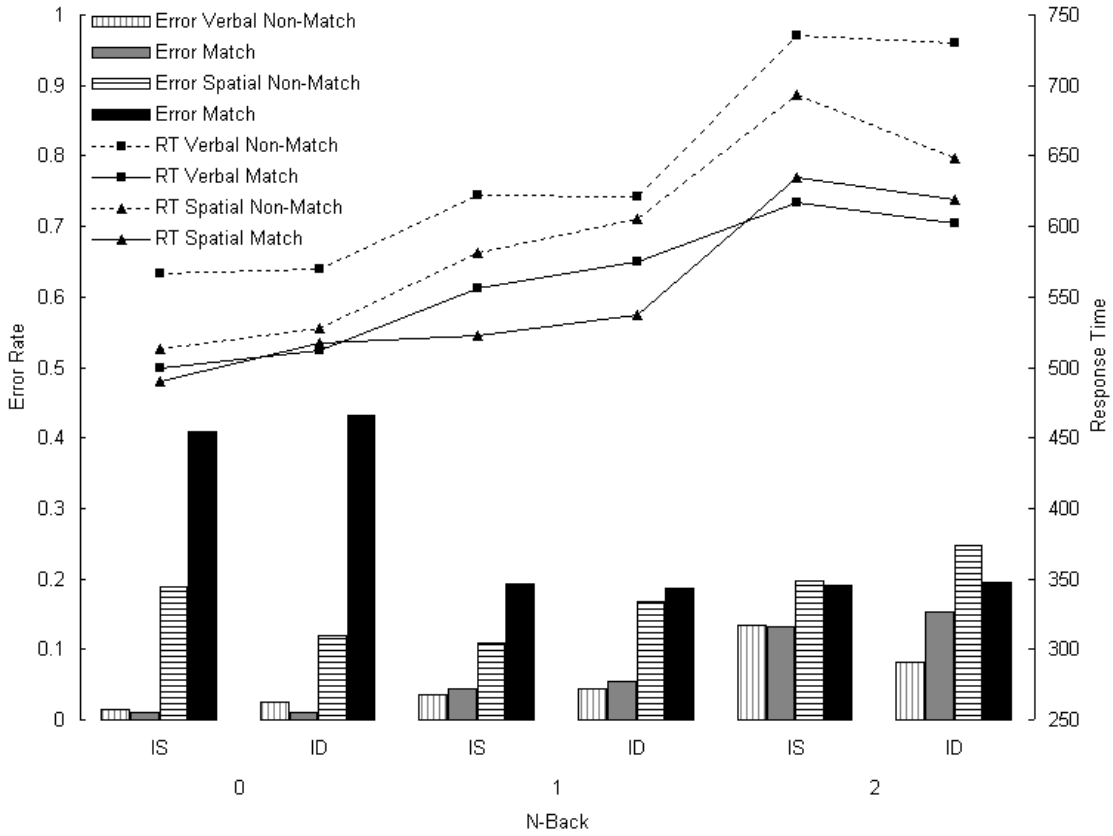

Figure 3-2. *Response time (lines) and error rate (bars) in 0-, 1-, and 2-back conditions, separately for ID and IS conditions, for spatial and verbal tasks, and for match and non-match trials.*

3.3.1. Behavioral data

Figure 3-2 shows all the behavioral data. Response time to match stimuli was

shorter than that to non-match stimuli, $F(1,10) = 13.53$, $p = .004$ and increased with increasing memory load $F(1.3,12.8) = 23.79$, $p < .001$. All F of other RT effects were lesser than 3.58 and all p were larger than .064. Error rate in spatial tasks were higher than in verbal tasks, $F(1,10) = 11.79$, $p = .006$. No other error rate-effects were significant. All F of other error-rate effects were lesser than 3.59 and all p were larger than .068.

3.3.2. Electrophysiological data

Figure 3-3 shows *t*-statistical maps of replacement effects. Figure 3-4 illustrates *t*-statistical maps of shift effects. Figure 3-5 demonstrates grand mean amplitudes of replacement (1-back minus 0-back difference) and shift (2-back minus 1-back difference) effects in every condition. The statistics on original ERPs are all non-significant. This could be because there were too few participants to obtain ERP effects, but enough to obtain difference waveform effects.

3.3.2.1. The t-statistical maps

The *t*-statistical maps provide intuitive pattern shows of information processing in replacement (see Figure 3-3). As shown in t-statistical maps, distractedness effects were obvious in spatial replacement. Interference began at around 200 ms after

stimulus onset in posterior regions, at around 400 ms in frontal regions, and lasted until the end of the epoch (800 ms). In contrast, distractedness effects were not obvious in verbal replacement. In general, amplitudes in ID tended to be more positive-going especially in the posterior areas. This tendency could not be seen in verbal replacement. However, a possible interpretation is that patterns in ID were about the same (generally negative) in both spatial and verbal replacement, but patterns in IS were quite different. In spatial replacement, a generally negative-going pattern could be seen in IS, whereas a posterior positive-going pattern was seen in ID. No obvious pattern change was observed as time went in both spatial and verbal replacement.

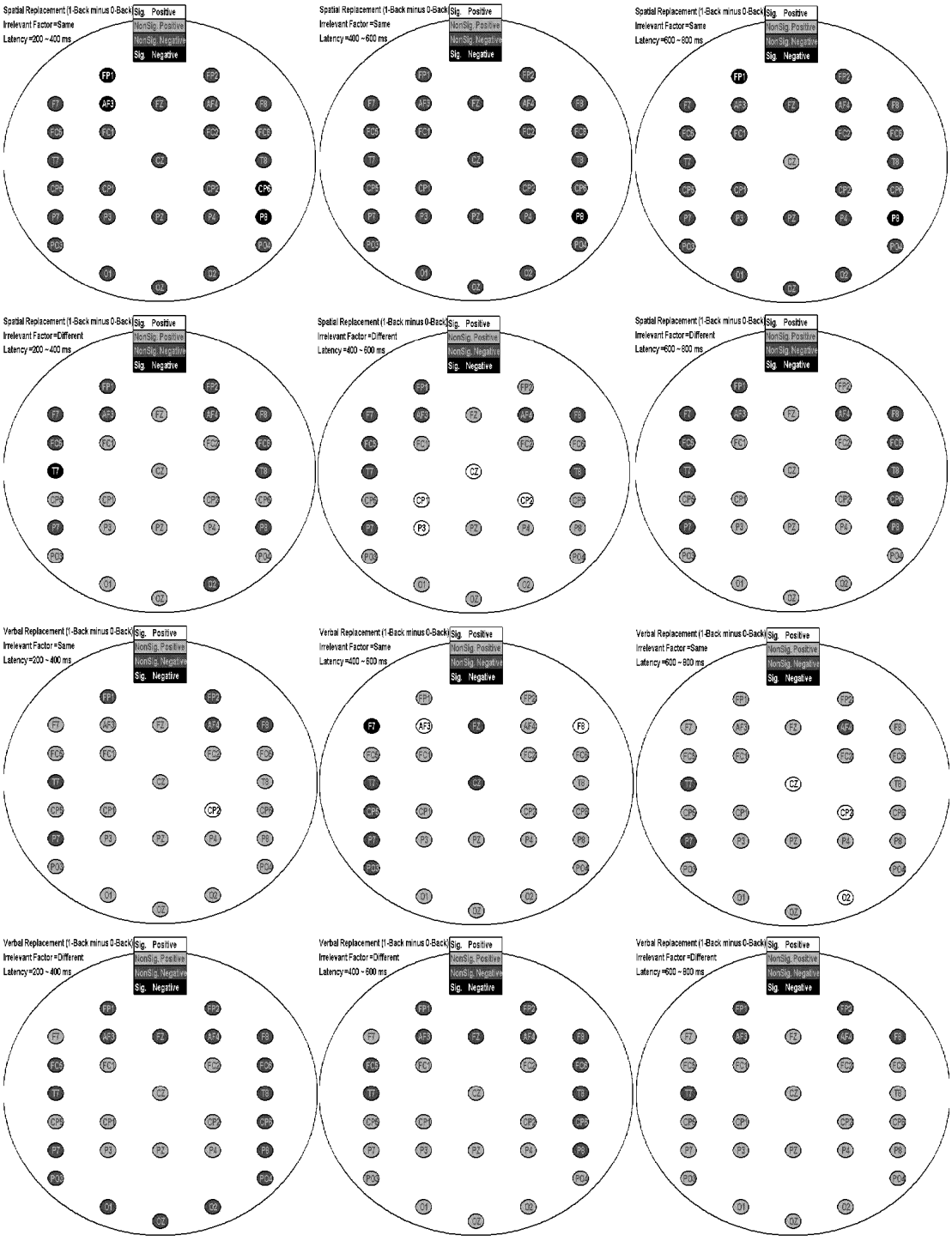

Figure 3-3. *The t-statistical maps demonstrate effects of spatial replacement elicited in IS (Row 1) and ID (Row 2) conditions, and verbal replacement elicited in IS (Row 3) and ID (Row 4) conditions, in successive three time windows: 200-400 ms (Column 1), 400-600 ms (Column 2) and 600-800 ms (Column 3). The white, light grey, dark grey and black labels represent significant positive-going, non-significant positive-going, non-significant negative-going and significant negative-going amplitudes in these electrodes.*

In spatial replacement, amplitudes in IS were significantly negative-going in particular electrodes, and sustained around left frontal and right parietal regions. In verbal replacement, in contrast, amplitudes in IS were significantly positive-going in particular electrodes. Interference began at around 200 ms after stimulus onset in posterior regions, at around 400 ms in frontal regions, and returned to posterior regions until the end of the epoch (800 ms). These significances were not seen in ID in verbal replacement. These results suggested that interference from the irrelevant domain 'blurred' ERP patterns in verbal replacement.

The pattern of shift effects (Figure 3-4) was quite different from that of replacement effects (Figure 3-3). Distractedness effects in spatial shift (Figure 3-4) were obvious only in some electrodes. Numerically, distractedness effects extended from 200 to 800 ms in FC5 and P3 and from 400 to 800 ms in Cz. In contrast to spatial replacement (Figure 3-3), distractedness effects in shift (Figure 3-4) tended to be unsystematic, for example, positive-going in P7 but negative-going in P3. Verbal shift also had not obvious distractedness effects.

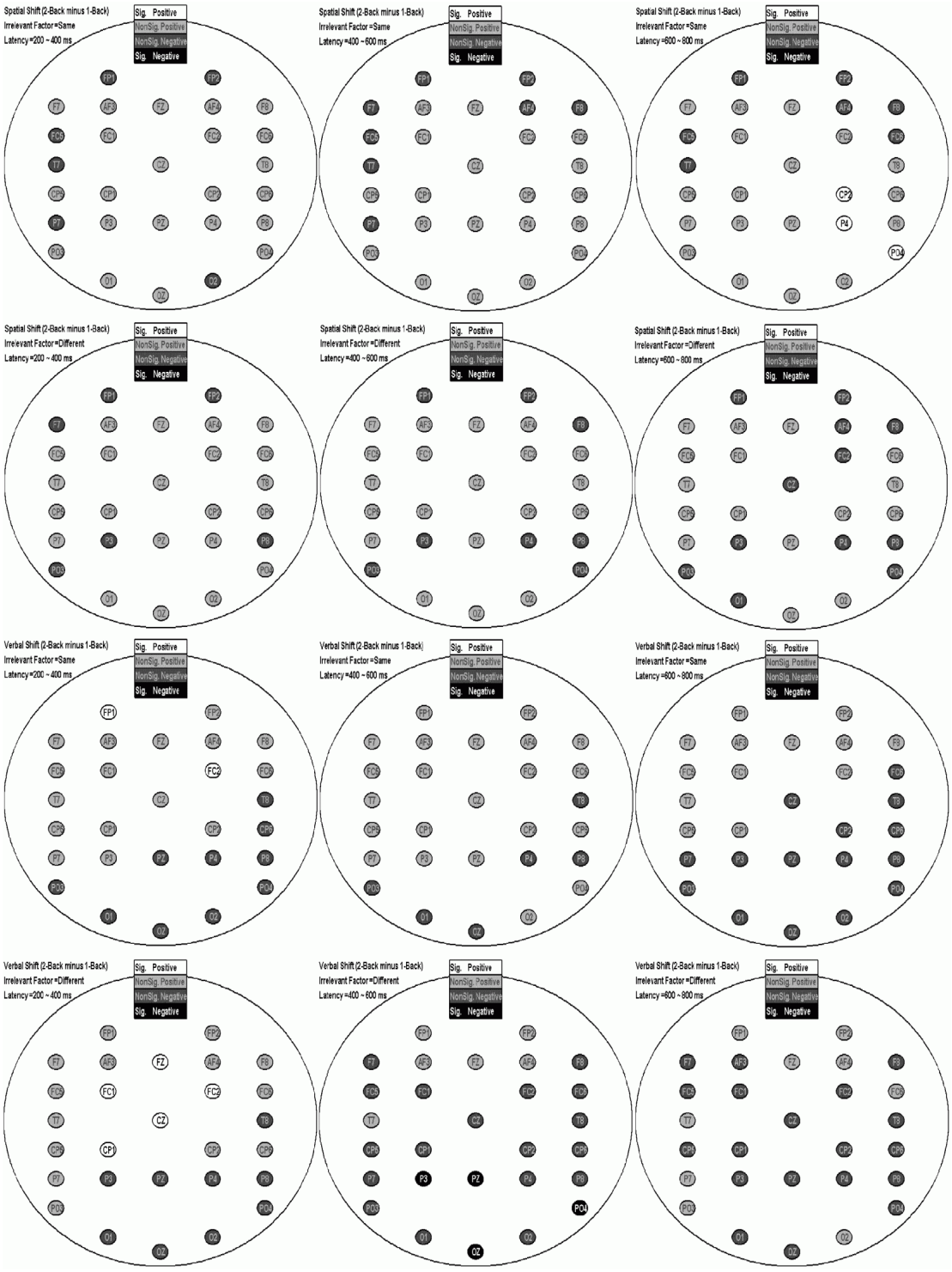

Figure 3-4. *The t-statistical maps demonstrate effects of spatial shift elicited in IS (Row 1) and ID (Row 2) conditions, and verbal shift elicited in IS (Row 3) and ID (Row 4) conditions, in successive three time windows: 200-400 ms (Column 1), 400-600 ms (Column 2) and 600-800 ms (Column 3). The white, light grey, dark grey and black labels represent significant positive-going, non-significant positive-going, non-significant negative-going and significant negative-going amplitudes in these electrodes.*

Generally speaking, amplitudes in spatial shift were generally positive-going both in IS and ID, in contrast to those in spatial replacement (Figure 3-3). Patterns in spatial shift (Figure 3-4) did not change much as time went. In contrast, amplitudes in verbal shift were also generally positive-going in IS, but negative-going in ID. As time went, amplitudes tended to be negative-going especially in the posterior regions, but this tendency was not very obvious.

In spatial shift (Figure 3-4), amplitudes in IS were significantly positive-going only at 600-800 ms in CP2, P4 and PO4 electrodes. In ID, the significance was not seen in all the thirty-two electrodes. In verbal shift, amplitudes in IS were significantly positive-going only at 200-400 ms in FP1 and FC2 electrodes. However, in ID at 200-400 ms, amplitudes were significantly positive-going in five electrodes. Furthermore, at 400-600 ms, amplitudes were significantly negative-going in four electrodes. The significant electrodes existed from frontal to occipital and from positive-going to negative-going as time went.

In this context, the relative smaller number of effects in Figure 3-3 as compared to study 1 could be due to a lack of power (especially considering that alpha levels are uncorrected for multiple comparisons).

3.3.2.2. ANOVA for replacement ERPs

A marginally significant Task effect (see Figure 3-5) was found in the time window 200-400 ms, where amplitudes were more negative going under spatial instructions than those under verbal instructions, $F(1, 10) = 3.33$, $p = .098$. In the time window 400-600 ms, amplitudes were more positive-going in ID than those in IS under spatial instructions, whereas amplitudes were more positive-going in IS than those in ID under verbal instructions, as evidenced by a marginally significant IF × Task interaction, $F(1, 10) = 4.39$, $p = .063$. Another marginally significant ACP effect showed that amplitudes were most positive-going in central electrodes and most negative-going in anterior electrodes, whereas those in posterior electrodes were amid them, $F(2, 20) = 3.81$, $p = .072$. The amplitude differences between ID and IS conditions increased from anterior to posterior electrodes, as evidenced by a significant IF × ACP interaction, $F(2, 20) = 13.22$, $p = .002$. Another significant IF × ACP interaction in the 600-800 ms time window revealed that the amplitude differences between ID and IS conditions increased from anterior to posterior electrodes, $F(2, 20) = 4.80$, $p = .042$. A marginally significant three-way IF × Hemisphere × Task interaction, $F(1, 10) = 4.17$, $p = .068$, revealed that amplitudes in ID were more negative-going than in IS in the left hemisphere but ID amplitudes were about the same as IS amplitudes under verbal instructions in the right hemisphere. Under spatial instructions, ID amplitudes were more positive-going than IS

amplitudes. Other effects and interactions in replacement were neither significant nor marginally significant. All *F* of other replacement effects were less than 3.24 and all *p* were larger than .101.

3.3.2.3. ANOVA for shift ERPs

Unlike replacement, all effects and interactions were neither significant nor marginally significant in ANOVA of 2-back minus 1-back amplitude difference (shift), all F of shift effects were lesser than 2.690 and all *p* were larger than .131.

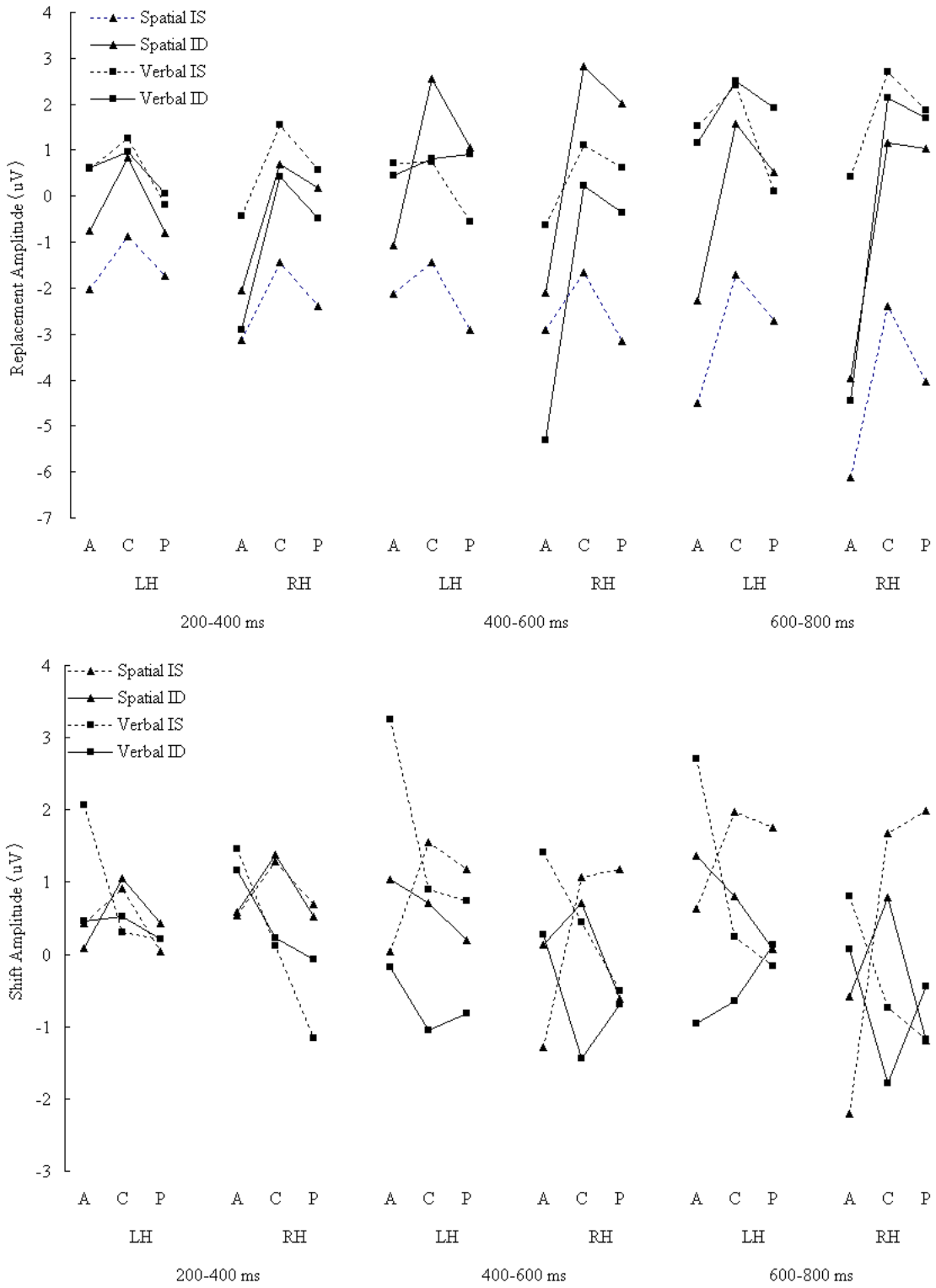

Figure 3-5. *Replacement (upper) and shift (lower) amplitudes elicited during spatial (triangle) and verbal (square) tasks. Solid lines indicate ERPs elicited under ID condition. Dashed lines indicate ERPs elicited under IS condition. A: Anterior; C: Central; P: Posterior; LH: Left Hemisphere; RH: Right Hemisphere.*

3.4. Discussion

In replacement, significant and marginally significant interactions with irrelevant features were found at 400-600 ms, and also significant interaction at 600-800 ms. These results indicate that cross-domain influence existed in replacement and lasted at least 800 ms in latency. The assumption, that a task with top-down control and cross-domain stimuli provides "pure" comparison between spatial and verbal information processing, is thus challenged.

From these interactions, the first hint is about the effect of instruction. At 400-600 ms, replacement-amplitudes were more positive-going in irrelevant-difference (ID) than those in irrelevant-simitry (IS) under spatial instructions, whereas replacement-amplitudes were more positive-going in IS than those in ID under verbal instructions. This pattern implicates that cross-domain interference did not depend on ID or IS, but on verbal or spatial. If the irrelevant domain was verbal (*i.e.*, under spatial instructions), replacement-amplitudes were more positive-going at 400-600 ms, and vice versa. Accompanying with the following fact that amplitudes at 200-400 ms were more negative-going under spatial instructions than those under verbal instructions, an interesting pattern emerges: replacement-amplitudes were more negative-going at 200-400 ms and turned to be more positive-going at 400-600 ms under spatial instructions, whereas

replacement-amplitudes were less negative-going at 200-400 ms and turned to be less positive-going at 400-600 ms under spatial instructions. The conclusion is that stimulus effects are stronger under verbal instructions than under spatial instructions.

The second hint is about functional anatomy. Amplitude differences between ID and IS conditions at 400-800 ms revealed that cross-domain influence was larger in posterior areas than frontal areas. As a result, frontal lobes are "relatively distractedness-free" areas in replacement.

Effects and interactions from irrelevant domains were not significant in shifts. Accompanying with the influences from the irrelevant domain shown in replacement, a hint is that such kind of influence is originated from perceptual process *per se* because replacement manipulates external stimuli but shift manipulates already-encoded information. Therefore, the assumption that identical stimuli eliminate difference in perceptual processes and provide pure comparison between spatial and verbal information processing may be wrong. Further, even for the identical stimuli, the input information in the perceptual processes has been adjusted by the pre-input illustration. Nevertheless, this speculation should be surveyed by further experiments.

Response time was longer in spatial tasks than in verbal tasks. Error rate was also higher in spatial tasks than in verbal tasks. Combining behavioral results

together suggests that spatial tasks are more difficult than verbal tasks. Response time prolonged with memory loads also suggests the similar effect, where 2-back task is more difficult than 1-back task, and 1-back task is more difficult than 0-back task. This conclusion provides reasonable explanation for the conclusion from EP results, where verbal effects were stronger than spatial effects (McEvoy *et al.*, 1998b). In this EP study, WM tasks elicited transient response reflecting different component of task processing. The transient responses, with the exception of P300, differed between spatial and verbal task versions. The P300 were not affected by task version but affected by increased WM load.

From visual inspection of *t*-statistical maps, interference from the irrelevant domain 'blurred' ERP patterns in verbal replacement. In contrast to verbal replacement, ERP patterns seem to be 'sharper' for ID in verbal shift. A possible explanation is that shift manipulates already-encoded information thus the irrelevant domain of a new stimulus has no direct influences in the shift process. The temporal pattern change in the spatial replacement implies information flow of posterior-anterior-posterior pattern, whereas the temporal pattern change in verbal shift implies unidirectional information flow from frontal to occipital areas. In comparison with the logical model of N-back tasks (see Figure 3-1), a possible speculation is that replacement is related to posterior areas and shift is related to

anterior areas, then information flows to the posterior area after all. Nevertheless, this speculation needs further experiments to testify.

3.5. Conclusion

Cross-domain interference from nominally irrelevant domains was observed in replacement. Thus, irrelevant domains are not really irrelevant. Consequently, even when identical stimulus displays are used to exclude perceptual effects, 'pure' comparison of spatial and verbal information processing in WM tasks is still not general but process-specific. Thus, it is important to take the cross-domain interference into account while drawing conclusions from neuropsychological experiments. Distractedness effects from nominally irrelevant domains were observed in replacement. Thus, irrelevant domains were not really irrelevant. Consequently, even when identical stimulus displays are used to exclude perceptual effects, 'pure' comparison of spatial and verbal information processing in WM tasks is impossible. We cannot rely on selective attention to reject influence in WM manipulation from the irrelevant domain. A promising alternative is to use data-driven control to cut the influence from the origin. To survey this issue, I arranged a corresponding experiment of the experiment one with data-driven control – Experiment 3.

Chapter 4. Experiment 3: Is information processing different between spatial and verbal stimuli in a data-driven task?

4.1. Introduction

The effects of cross-domain interference on N-back task performance (or its cortical correlates) have been shown in Experiment 2. In that, a potential confound in Experiment 1, which use the same (verbal) stimuli (e.g., letters of the alphabet) in both the verbal and spatial task conditions, should be taken into account. Given the type of results obtained by (Meegan *et al.*, 2004), it is possible that cross-domain interference may play a role in verbal vs. spatial task conditions when the stimuli can be encoded for both verbal and spatial characteristics simultaneously. For example, if the stimuli in the N-back task are words or letters of the alphabet, and participants are performing in the spatial task condition (i.e., matching location), is their performance affected by whether or not letter or word identity matches with the stimulus n presentations back?

In Experiment 3, the verbal and spatial WM conditions were better isolated by using word stimuli in the verbal matching conditions and the same non-verbal location marker in the spatial location matching conditions. Data were analyzed in two steps. First, the general pattern of ERP effects associated with the spatial and verbal versions of the task was examined, expecting to replicate earlier findings such as reduced P3 amplitude under higher WM load conditions (McEvoy *et al.*, 1998b). A question of particular interest was how the different stimuli in the spatial vs. verbal

conditions would alter cortical correlates. If the stimuli elicited domain-specific processing, the verbal condition could be expected to show neural activity predominantly in the left hemisphere, whereas the spatial condition should show neural activity predominantly in the right hemisphere (Beauregard *et al.*, 1997; Deutsch *et al.*, 1988; Petersen *et al.*, 1990).

Second, differences in ERP patterns were closely examined between the levels of the N-back task. Based on the task analysis presented above, ERP differences were expected between 1-back and 0-back conditions to specifically reflect the physiological correlates of the replacement operation, and differences between the 2-back and 1-back conditions to reflect effects of increasing maintenance load and the shift operation. Again, to the extent that the different stimuli in the verbal vs. spatial condition elicited domain-specific processing, these effects could show domain-specific lateralization (Smith & Jonides, 1997).

4.2. Method

4.2.1. Participants

Thirty paid volunteers (15 female) ranging in age from 18 to 34 (mean 22) years participated in the experiment. According to self-report, all had normal or

corrected-to-normal vision, and all except six participants were right-handed.

4.2.2. Stimulus and apparatus

Stimulus presentation and data acquisition were managed by C-programs and running under MS-DOS. Behavioral data were saved on the hard disk.

Stimuli in the verbal condition were 20 words with similar frequency and length, whereas stimuli in the spatial condition were strings of $ symbols of matched length. Words were presented in white on black on a 17" computer monitor, at one out of eight circularly arranged positions 4° from the screen centre. Words had a height of approximately 0.8° visual angle, and their width ranged from 3.2° to 6.4° (mean: 5°).

4.2.3. Procedure

Participants were seated in an armchair in front of a computer screen at distance of approximately 60 cm. They were told to keep a comfortable posture, and to avoid eye movements and eye blinks during experimental trials. Participants then completed the first half of the experiment, comprising six blocks of N-back tasks, followed by a break, during which participants were encouraged to leave the experimental room. They then completed the second half of the experiment.

Each half of the experiment consisted of two 0-back blocks, two 1-back blocks,

and two 2-back blocks in sequence. In the first half, each pair of blocks was preceded by a corresponding practice block, so as to familiarize participants with the changing task requirements. In the second half, no practice blocks were given. Experimental blocks consisted of 64 trials (32 matching trials and 32 non-matching trials). Each trial began with the presentation of a fixation cross in the centre of a screen for 350 ms, followed by 350 ms of a blank screen. In the verbal task, a stimulus word was then shown for 500 ms at the screen centre. In the spatial task, a string of $ signs was then shown for 500 ms at one of the eight predefined screen location. This was followed by another blank screen for 1500 ms (see Figure 4-1). In all blocks, identity in verbal tasks and location in spatial tasks of each stimulus were determined pseudo-randomly, to achieve an approximately even distribution of targets and an approximately equal distribution of identities or locations. Practice blocks were constructed in the same way, but contained only 20 trials and provided additional feedback (the words “correct” or “wrong” presented in the centre of the screen) immediately after the participant’s response. Data from practice blocks was not saved.

In the 0-back task, participants indicated whether or not each stimulus matched the first one of the block. For the more demanding levels of the N-back task, participants had to match the current stimulus with the previous stimulus (1-back task)

or the stimulus before the previous one (2-back task). Participants pressed a "yes" key for a match (matching stimulus) and a "no" key for a mismatch (non-matching stimulus). Keys were "\"and "/" keys of a computer keyboard, which had to be pressed with the left and right index finger, respectively. Participants were asked to respond as quickly and accurately as possible, and assignment of keys to "yes" and "no" response was counterbalanced across participants.

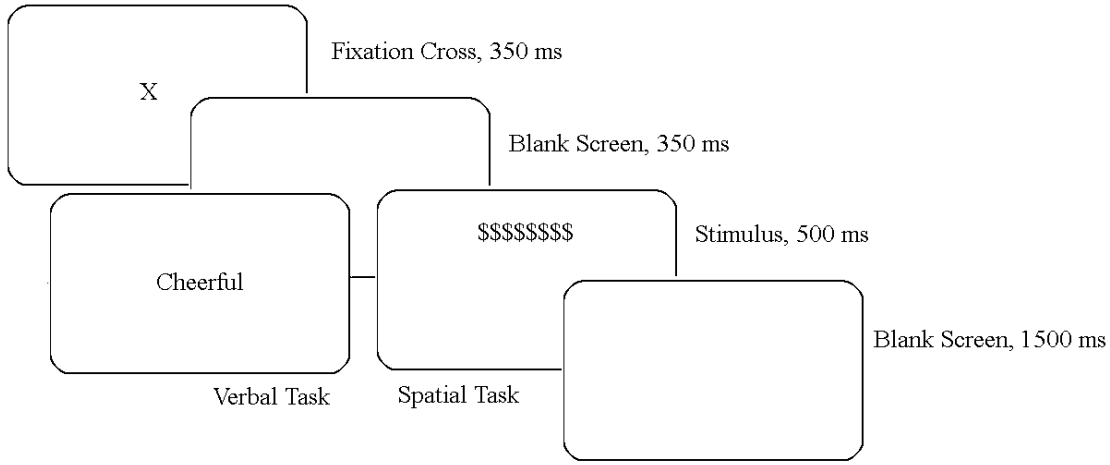

Figure 4-1. *Experimental trial*

Two different versions of the N-back task were employed, and participants were assigned randomly to either of these. In the verbal version, the task-relevant feature of the stimulus words was their identity. In the spatial version, the location of the stimulus on the screen was task-relevant.

4.2.4. Electrophysiological recording and data processing

Using a BioSemi Active-Two amplifier system, continuous EEG recordings were made with Ag / AgCl electrodes, mounted on a nylon cap, from 32 locations of the international 10–20 system (left: Fp1, AF3, F7, F3, FC1, FC5, T7, C3, CP1, CP5, P7, P3b, PO3, O1; midline: FZ, CZ, PZ,OZ; and corresponding right channels). Sampling rate was 256 Hz. EEG signals were off-line filtered using a 0.01 Hz high pass and a 30 Hz low pass filter, and were re-referenced to linked earlobes.

Further analysis was conducted using EEGLAB 4.43 (Delorme & Makeig, 2004) under MATLAB 6.1 environment. EEGs were averaged off-line for epochs of 900 ms, starting 100 ms prior to stimulus onset, and ending 800 ms afterwards. Trials containing saccadic eye movement or eye blinks (indicated by amplitudes beyond 3 SD in single channel and 1.5 SD in all channels), and trials where participants gave an incorrect response, were excluded from analysis. EEG on correct-response trials was averaged for each condition separately, relative to a 100-ms pre-stimulus baseline. Thus for each participant, six ERP waveforms were constructed one matching ERP and one non-matching ERP from each of the 0-back, 1-back, 2-back task.

4.2.5. Behavioral data

All the behavioral data including response time (RT) and error rate were analyzed by

a repeated-measure ANOVA. The between-subject factor for behavioral data in the ANOVA was Task (spatial / verbal). The within-subject factors were Stimulus (non-matching / matching) and N-Back (0 / 1 / 2).

4.2.6. ANOVA of general ERPs

Based on visual inspections of the grand mean waveforms, four latency windows were selected for analysis: EPC (early-posterior complex, 150-250 ms) in posterior areas (non-midline: P3, P4, P7, P8, O1, O2, PO3, PO4; midline: Pz, and Oz), further referred to as early posterior complex (EPC); 200-300 ms in anterior areas (non-midline: FP1, FP2, AF3, AF4, F7, F8, FC1, FC2, FC5, and FC6; midline: Fz and Cz), further referred to as P2a; a negative-going shift at 300-400 ms in anterior areas (non-midline: FC5/6, F7/8, FC1/2, AF3/4, FP1/2; midline: Fz, Cz), further referred to as N2; and 300-500 ms in central-posterior areas (non-midline: FC1, FC5, C3, T7, CP1, CP5, P3, P7, O1, PO3, and corresponding contralateral channels; midline: Cz, Pz, and Oz), further referred to as P3. ERP component amplitudes, which were defined as mean amplitudes within certain time window, were analyzed separately using a repeated-measure ANOVA with the between-subject factor Task (verbal / spatial), and with the within-subject factors Stimulus (non-matching / matching) and N-Back (0 / 1 / 2), and the factor Hemisphere (left / right) only in non-midline

channels.

4.2.7. ANOVA of replacement and shift effects

Based on visual inspections of the difference waveforms, electrodes in frontal (F7, F8, AF3, AF4), temporoparietal (C3, C4, T7, T8), and parietal areas (P3, P4, P7, P8) at 200-400, 400-600 and 600-800 ms post stimulus were selected for analysis. The replacement/shift effects were analyzed separately using a repeated-measure ANOVA with the between-subject factor Task (verbal / spatial), and with within-subject factors Hemisphere (left / right), ACP (anterior/ central/ posterior) and Stimulus (matching/ mismatching).

4.3. Results

4.3.1. Behavioral data

Figure 4-2 presents RT and error rate.

Response time in the spatial task was larger than in verbal task, as evidenced by a significant Task effect, $F(1, 28) = 8.40$, $p = .007$. RT to matching stimuli was larger than to non-matching ones, as evidenced by a significant Stimulus effect, $F(1, 28) = 147.32$, $p < .001$. RT differences between matching and non-matching stimuli

were larger in spatial tasks than in verbal tasks, as evidenced by a significant Stimulus × Task interaction, $F(1, 28) = 6.15$, $p = .019$. RT increased with increasing memory loads, as evidenced by a significant N-Back effect, $F(2, 56) = 44.85$, $p < .001$. RT differences between matching and non-matching stimuli were largest in 2-back tasks than in 0- and 1- back tasks, as evidenced by a significant Stimulus × N-Back effect, $F(2, 56) = 30.82$, $p < .001$. Other main effects or interactions were non-significant in RT, all $F < 2.23$, all $p > .133$.

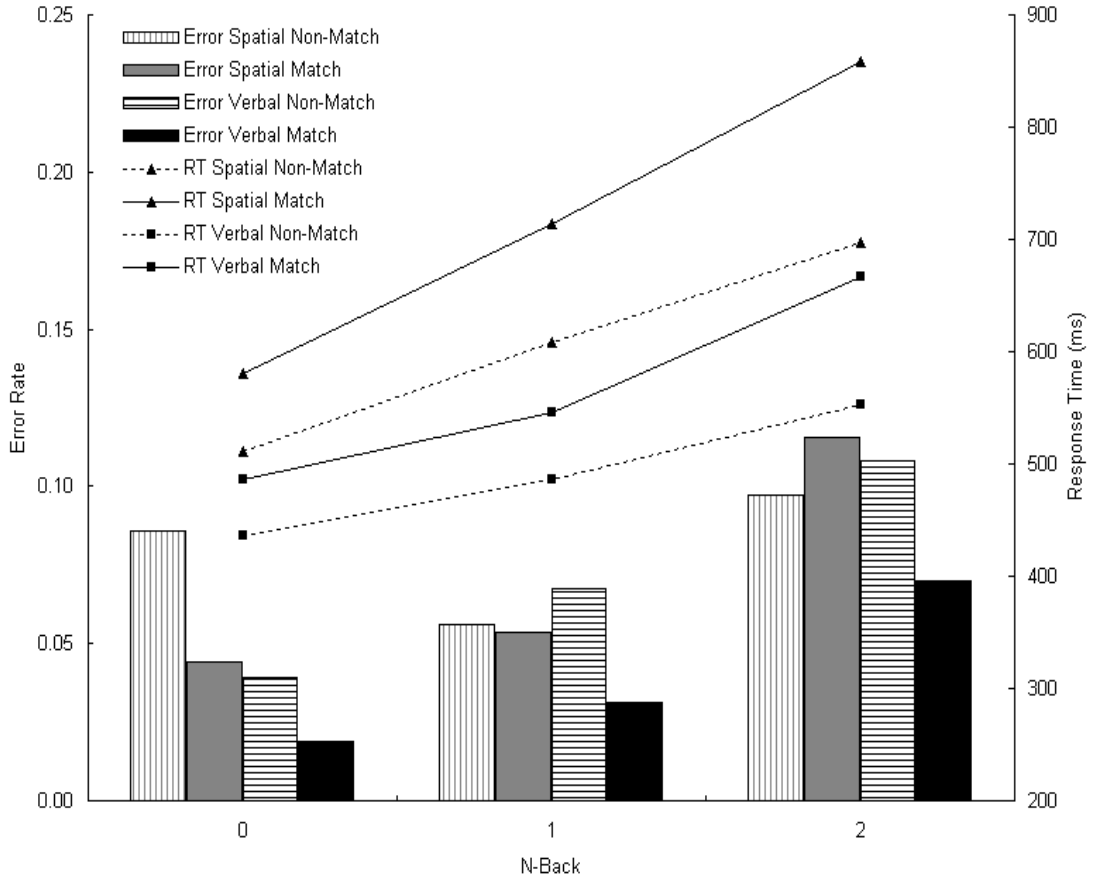

Figure 4-2. *Response time (lines) and error rate (bars) in 0-, 1-, and 2-back conditions, separately for spatial and verbal tasks, and separately for match trials and non-match trials.*

Error rate increased as a function of memory load, as evidenced by a significant N-Back effect, $F(2, 56) = 14.46$, $p < .001$. Other main effects or interactions were non-significant in error rate, all $F < 3.80$, all $p > .060$.

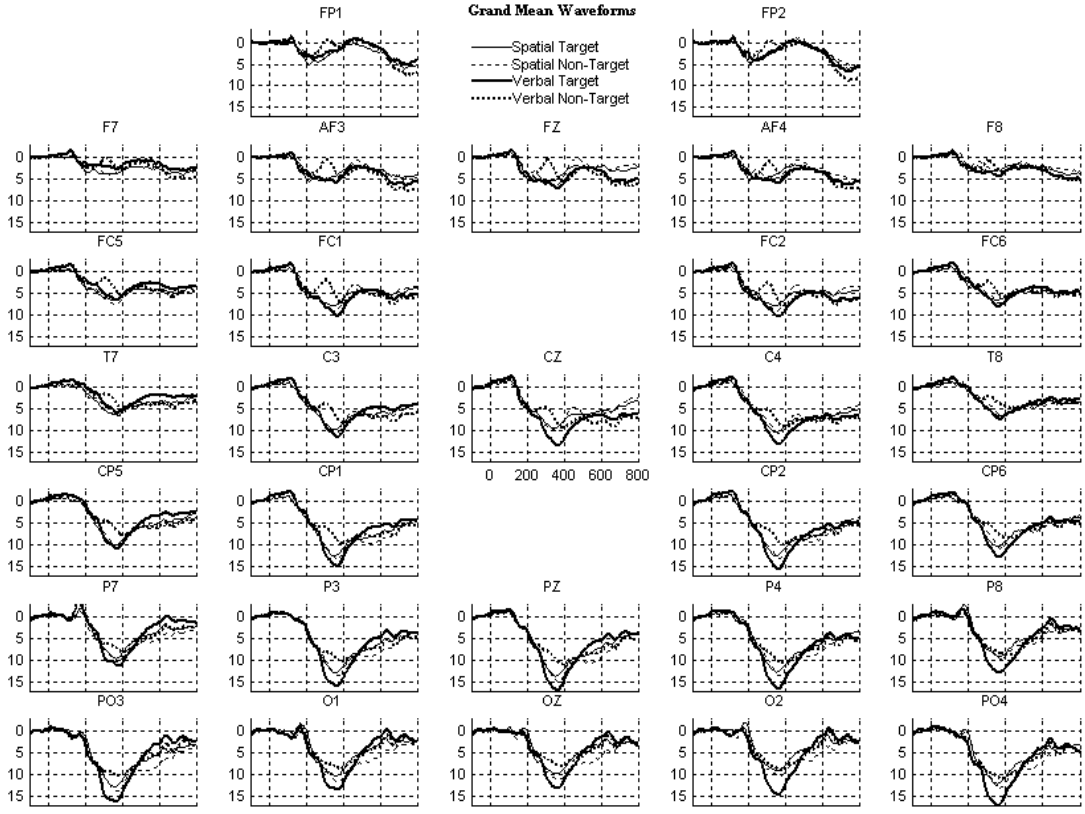

Figure 4-3. *Grand mean ERP waveforms, collapsed across the N-back factor, elicited during spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

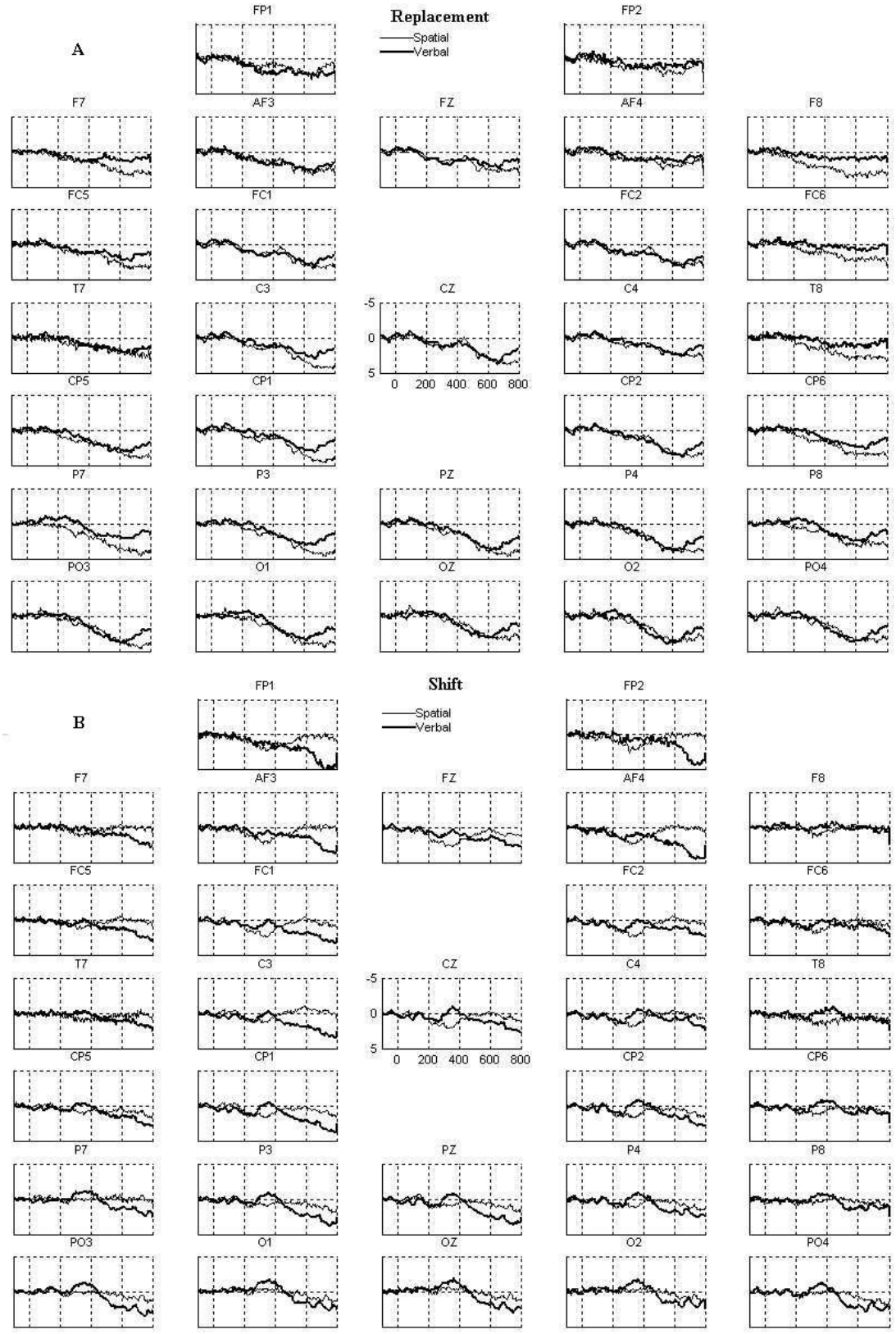

Figure 4-4. *Replacement (1-back minus 0-back difference waveforms, A) and shift effects (2-back minus 1-back difference waveforms, B), separately for spatial (thin line) and verbal (think line) stimuli, collapsed across stimulus types (match and non-match).*

4.3.2. Electrophysiological data

Figure 4-3 presents grand mean ERP waveforms collapsing the N-back factor in 28 channels. Figure 4-4 demonstrates 1- minus 0-back difference waveforms (replacement) and 2- minus 1-back difference waveforms (shift) collapsing the Stimulus factor in 28 channels.

4.3.2.1. Omnibus ANOVA for Original ERPs

Table 4-1 shows *F* and *p* values from the omnibus ANOVA. Figure 4-5 demonstrates mean amplitudes in each ERP component.

The Stimulus effect was significant in P2a, N2 and P3 latency windows, but non-significant in the EPC component. Amplitudes in these latency windows were more positive-going for matching stimuli than for non-matching ones. The Stimulus × Task interaction was significant in N2 and P3. The amplitude differences in these latency windows between matching and non-matching stimuli were larger in verbal tasks than in spatial ones.

The N-Back factor was significant in P2a and N2 latency windows in both midline and non-midline channels, and non-midline P3 latency window. In general, amplitudes increased with increasing load. Increases in amplitude from 0- to 1-back tasks were smaller than those from 1- to 2-back tasks in anterior latency windows (the midline P3a). Conversely, amplitude increases from 0- to 1-back tasks were larger

than those from 1- to 2-back tasks in posterior latency windows (the non-midline P3). The N-Back × Task interaction was non-significant in all the latency windows.

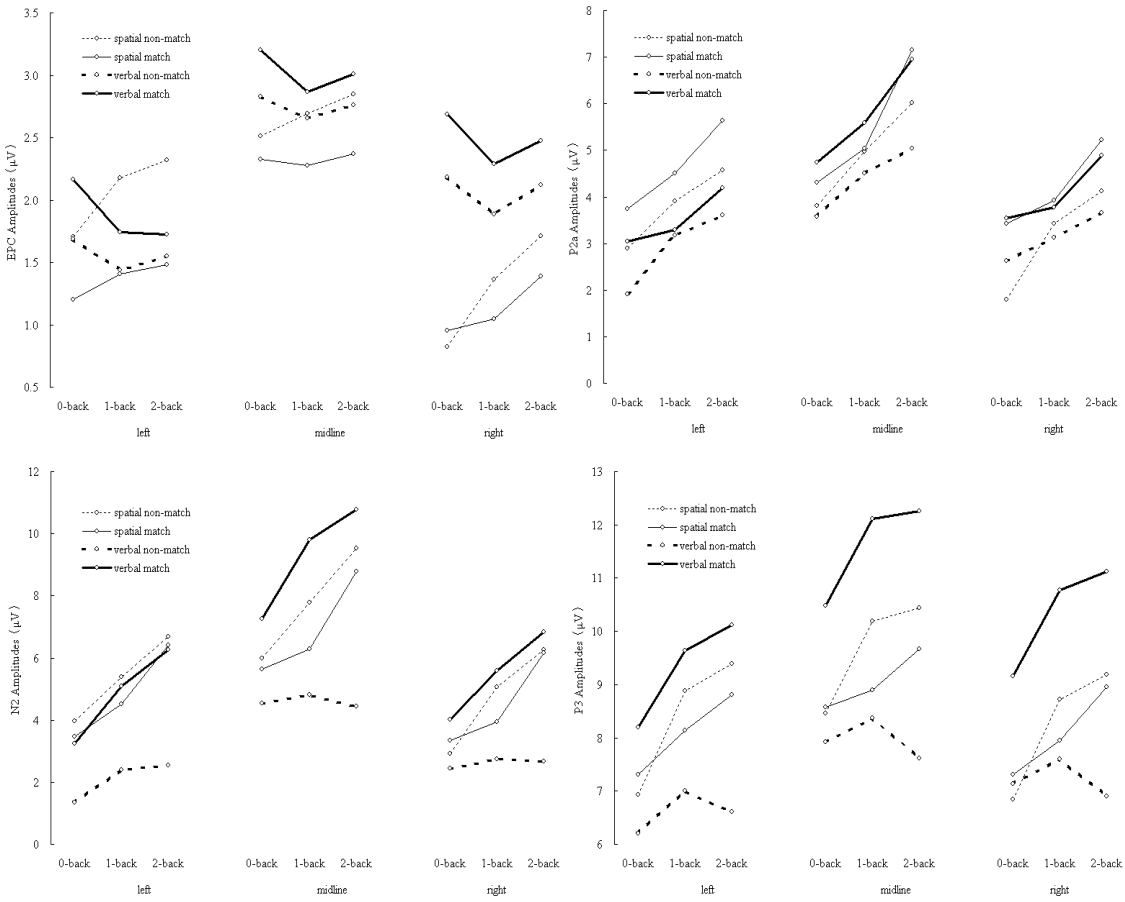

Figure 4-5. *Mean amplitudes in EPC (150-200 ms,), P2a (200-300 ms), N2 (300-400 ms), P3 (300-500 ms) latency windows elicited during for spatial (thin lines) and verbal (thick lines) tasks. Solid lines indicate ERPs elicited by matching items. Dashed lines indicate ERPs elicited by non-matching items.*

The analyses below involving the Hemisphere factor only cover the non-midline channels. The Hemisphere effect and Hemisphere × Stimulus interaction were non-significant in all the four latency windows. The Hemisphere × Task interaction was significant in all the latency windows except P3. In spatial tasks, amplitudes

were higher in the left hemisphere than in the right one, whereas in verbal tasks, amplitudes were higher in the right hemisphere than in the left one. The Hemisphere × N-Back interaction was non-significant in all the latency windows.

			EPC			P2a			N2			P3		
	Effects	dF	*F*	*p*		*F*	*p*		*F*	*p*		*F*	*p*	
non-midline	Hemisphere	(1,28)	0.013	0.909		0.193	0.664		0.051	0.824		2.525	0.123	
	Hemisphere × Task	(1,28)	5.089	0.032	*	6.958	0.013	*	4.223	0.049	*	3.784	0.062	
	NBack	(2,56)	0.219	0.782		8.471	0.002	*	9.475	0.001	*	4.236	0.027	*
	NBack × Task	(2,56)	0.933	0.391		0.331	0.651		0.672	0.488		0.427	0.614	
	Stimulus	(1,28)	0.028	0.868		8.802	0.006	*	16.049	0.000	*	20.523	0.000	*
	Stimulus × Task	(1,28)	4.068	0.053		0.099	0.755		28.581	0.000	*	28.565	0.000	*
	Hemisphere × NBack	(2,56)	1.278	0.284		0.380	0.668		0.467	0.605		0.307	0.698	
	Hemisphere × NBack × Task	(2,56)	0.051	0.923		1.662	0.201		1.895	0.165		0.574	0.538	
	Hemisphere × Stimulus	(1,28)	3.324	0.079		3.304	0.080		0.635	0.432		1.642	0.211	
	Hemisphere × Stimulus × Task	(1,28)	1.528	0.227		0.056	0.815		0.171	0.683		0.409	0.528	
	NBack × Stimulus	(2,56)	0.513	0.594		2.559	0.089		4.615	0.015	*	1.802	0.178	
	NBack × Stimulus × Task	(2,56)	0.061	0.935		0.003	0.996		5.298	0.008	*	7.499	0.002	*
	Hemisphere × NBack × Stimulus	(2,56)	0.064	0.932		0.192	0.819		1.099	0.338		1.946	0.155	
	Hemisphere × NBack × Stimulus × Task	(2,56)	0.277	0.751		8.439	0.001	*	5.408	0.008	*	0.910	0.404	
midline	NBack	(2,56)	0.079	0.916		13.771	0.000	*	7.882	0.002	*	2.080	0.142	
	NBack × Task	(2,56)	0.155	0.845		0.421	0.612		1.265	0.287		0.285	0.720	
	Stimulus	(1,28)	0.033	0.857		6.277	0.018	*	29.418	0.000	*	18.815	0.000	*
	Stimulus × Task	(1,28)	1.940	0.175		1.121	0.299		61.790	0.000	*	38.704	0.000	*
	NBack × Stimulus	(2,56)	0.180	0.827		2.974	0.065		5.245	0.009	*	1.373	0.262	
	NBack × Stimulus × Task	(2,56)	0.023	0.974		0.102	0.885		9.158	0.000	*	6.321	0.005	*

Table 4-1. *Omnibus ANOVA for original ERPs (Task = verbal versus spatial task; Stimulus = matching versus non-matching stimulus; Hemisphere = left versus right hemisphere; N-Back = 0-back versus 1-back versus 2-back task; M, L = Midline versus Lateral Electrode Sites). Significant effects ($p < .05$) are marked with star.*

4.3.2.2. Omnibus ANOVA for replacement

Replacement effects (see Figure 4-4A) were significant only in posterior areas, and

after 400 ms in both spatial and verbal tasks. Replacement amplitudes were largest in anterior areas and smallest in posterior areas in the time window 200 – 400 ms (see Figure 4-6A), as evidenced by a significant ACP effect, $F(2,56) = 3.75$, $p = .043$. A borderline significant Stimulus × Task interaction also at 200-400 ms revealed that amplitudes responding to matching stimuli were larger than those to non-matching ones in verbal tasks, whereas amplitudes responding to matching stimuli were smaller than those to non-matching ones in spatial tasks, $F(1,28) = 4.12$, $p = .052$. At 600-800 ms, a significant Hemisphere effect showed that amplitudes in the left hemisphere were larger than those in the right hemisphere, $F(1,28) = 4.74$, $p = .038$.

A significant ACP × Hemisphere × Task interaction was found at 200 – 400 ms, $F(2,56) = 3.68$, $p = .032$. Lateralization as a function of task type was noted in anterior areas, where amplitudes in response to spatial stimuli were higher in the right hemisphere than in the left one and those to verbal stimuli were higher in the left hemisphere than the right one. Lateralization as a function of task type was also noted in the posterior areas but in a reversed pattern–amplitudes in response to spatial stimuli were higher in the left hemisphere and those to verbal stimuli were higher in the right hemisphere.

Significant Stimulus × Hemisphere × Task interactions were found at 200 – 400 ms, $F(1,28) = 5.86$, $p = .022$, and in the time window 600 – 800 ms, $F(1,28) = 4.66$, p

= .004. At 200 – 400 ms, lateralization as a function of task type was found in response to non-matching stimuli–amplitudes in response to spatial stimuli were higher in the right hemisphere than in the left one, and those in response to verbal stimuli were higher in the left hemisphere than the right one. In response to matching stimuli, lateralization as a function of task type was also noted but in a reverse pattern – amplitudes in response to spatial stimuli were higher in the left hemisphere and those in response to verbal stimuli were higher in the right hemisphere. At the 600 – 800 ms time window, relationships in response to matching stimuli were about the same as at 200 – 400 ms time window, but no lateralization to task type was found in response to non-matching stimuli.

There were significant ACP × Stimulus × Hemisphere interactions at 400 – 600 ms, $F(2,56) = 4.53$, $p = .021$, at 600 – 800 ms, $F(2,56) = 5.17$, $p = .012$, but the interaction was non-significant at 200 – 400 ms, $F(2,56) = 3.18$, $p = .058$. Lateralization as function of stimulus was found in the anterior areas–amplitudes in response to non-matching stimuli were higher in the right hemisphere than in the left one and those in response to matching stimuli were higher in the left hemisphere than in the right. Lateralization as a function of stimulus was also noted in the posterior areas but in a reverse pattern – amplitudes in response to non-matching stimuli were higher in the left hemisphere than in the left one and those to matching stimuli were

higher in the right hemisphere than in the left. At 600 – 800 ms, lateralization in anterior areas was not found, but it was still found in posterior areas.

Other effects in replacement were non-significant, $F < 3.21$, $p > .053$.

4.3.2.3. Omnibus ANOVA for shift

Shift effects (see Figure 4-4B) had different patterns. In spatial tasks, significant effects existed in all the areas at 200-400 ms, but only in frontal areas in 400-600 ms. After 600 ms, no significant effects were found. In verbal tasks, significant effects were found in frontal areas at 200-400 ms, and in posterior areas at 600-800 ms.

Shift amplitudes were largest in central areas and smallest in posterior areas in the time window 200 – 400 ms (see Figure 4-6B), as evidenced by a significant ACP effect, $F(2,56) = 5.92$, $p = .009$. A significant Stimulus effect in the time window 200 – 400 ms revealed that amplitudes were larger in the matching than the non-matching condition, $F(1,28) = 10.42$, $p = .003$. Other effects in shift were non-significant, $F < 3.01$, $p > .093$.

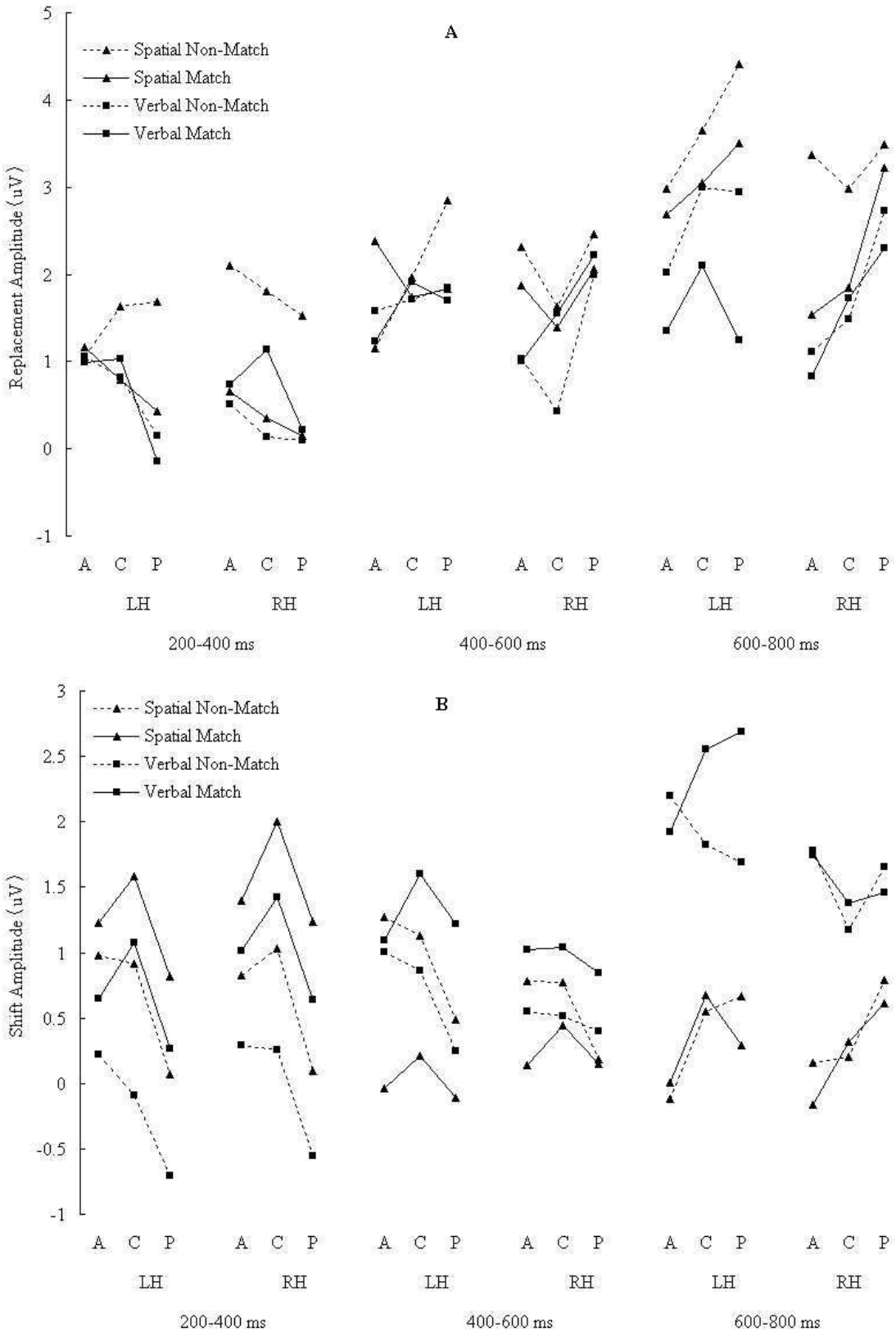

Figure 4-6. *Replacement (A) and shift (B) amplitudes elicited during spatial (triangle) and verbal (square) tasks. Solid lines indicate ERPs elicited by matching item. Dashed lines indicate ERPs elicited by non-matching items. A: Anterior; C: Central; P: Posterior; LH: Left Hemisphere; RH: Right Hemisphere.*

4.4. Discussion

The present experiment investigated the electrophysiological correlates of verbal and spatial WM in the N-back task with varying information processing load. In the following, we will first discuss the overall ERP effects of task instruction and memory load. Subsequently, we will consider the ERP evidence for distinct sub-processes in the N-back task and their possible differences depending on task instructions.

4.4.1. Electrophysiological correlates of verbal and spatial WM

The original response of N-back tasks reflects matching because memorization is logically immobilized and executed in the background. The average RT (595 ms) suggests the latest limit of matching sub-process. Within RT ranges, EPC amplitudes (in the similar time window as N1 and P1) were loading-constant, but loading effects were found in other latency windows. The significant P2a match effects were only found in verbal tasks, and suggested due to overlap with the negative-going N2. The N2 peaks were only seen in verbal non-match stimuli and significant “non-match” effects were seen. In contrast, P3 match effects were seen only in verbal tasks. Interestingly, no significant match effects were found in spatial tasks. The expected domain-specific lateralization was found in EPC, P2a and N2 time windows, but not in P3.

Loading-constant character in EPC hints that memory processing did not affect early activity in posterior cortex because loading-constant is the character of matching subtask whereas loading effects is the character of memory processing (Watter *et al.*, 2001). Nevertheless, it is possible that matching sub-process existed in EPC. By setting frequency of match stimuli equal to frequency of non-match ones, P3 effects only in verbal tasks were suggested from matching (McEvoy *et al.*, 1998b) rather than from infrequency. This result was also consistent with ERP experiments which surveyed spatial and verbal WM by item-recognition tasks (Ruchkin *et al.*, 1992). The distribution of domain-specific lateralization contrasts with the assumption that WM is a unitary mechanism which is not subdivided into modality-specific subsystems (e.g., Malhotra et al., 2005) and appear to be more in line with earlier findings of domain-specific lateralization even when stimulus material is held constant (Smith & Jonides, 1997).

To sum up, EPC, P2a and N2 were influenced by domains of stimuli but P3 was not. In contrast, P2a, N2 and P3 were influenced by match factors but EPC was not. In other words, the domain-specific attribute took effects before P3 whereas the match-specific attribute was given before P2a. Because match-specific attribute (match/non-match) must be given via matching sub-process and domain-specific attribute (spatial/verbal) caused lateralization only during perception, this provides

hints, although somewhat speculative, that matching takes place before 200 ms and the perception ends before 300 ms.

4.4.2. Sub-processes of WM

Unlike in Experiment 1, where identical stimuli formed the basis of spatial and verbal versions of the N-back task defined by instruction, the task in the present experiment was data-driven in that stimuli in the verbal version were words (with no spatial variation in presentation), and stimuli in the spatial version were matched strings of $ signs (with spatial variation in presentation). By our hypothesis, the replacement sub-process of the task is data-driven whereas the shift sub-process is conceptual. As can be seen in Table 1, the vast majority of electrophysiological effects of experimental manipulations in the present experiment were in the replacement sub-process. This is in clear contrast to Experiment 1, where the effects were concentrated on the shift sub-process. In the present experiment, it was the replacement sub-process that was left-lateralized for verbal, and right-lateralized for spatial stimuli. This was the pattern in the anterior area, but it was curiously the reverse in the posterior area.

In terms of the anterior-posterior distribution of the replacement and shift sub-processes, the results showed relatively greater posterior involvement in

replacement than in shift, as would be expected from our hypothesis. However, our predictions did not fare as well for anterior and central area activity - anterior amplitudes were the highest in replacement, whereas central amplitudes were greater in shift (whereas we would have predicted posterior and anterior areas to have the highest amplitudes in replacement and shift, respectively. It is possible that the match effects that are discussed below had an influence on this pattern. Behavioral data showed increasing RT (and decreasing accuracy) with increasing N, as was found in Experiment 1. Also, RT in the spatial task was longer than in the verbal task. This effect was not found in Experiment 1, but is explicable in terms of differences in the task requirements between the two experiments – in the present experiment, performing the spatial task involved making eye movements to various locations within the display, whereas this was not the case for centrally presented stimuli in the verbal task. However, Experiment 1 did produce more errors in the spatial task, despite identical stimuli and their spatial distribution in both versions of the task. It is therefore possible that the accuracy effect in Experiment 1 and RT effect in Experiment 3 both point to the spatial task being harder than the verbal task.

As in Experiment 1, and contrary to our logical task analysis, the outcome of the matching sub-process had a complex impact on the electrophysiology of subsequent sub-processes. Unlike in Experiment 1, where it was the shift sub-process that was

most affected, the impact of matching was much more concentrated on the replacement sub-process in the present experiment. In the earliest of the time windows examined (200-400 ms post-stimulus), replacement amplitudes for non-match stimuli were left-lateralized for verbal and right-lateralized for spatial stimuli, as would be expected based on the nature of the tasks. For match stimuli, however, this pattern was reversed, something that was also found the 600-800 ms time window as well. A similar reversal was found in the two later time windows between anterior and posterior areas in the replacement sub-process. In the anterior area, processing of match stimuli in the 400-600 ms time window was left-lateralized and of non-match stimuli was right-lateralized. In the posterior area, this pattern was reversed, and was significant also in the 600-800 ms time window.

It seems clear from the match effects observed here and in Experiment 1 that the matching sub-task of N-back tasks has a measurable impact on replacement and shift sub-processes across a wide latency range. These results are not consistent with our logical task analysis, in which the matching component of each trial is assumed to precede replacement and shift in an encapsulated manner. A possible explanation for the observed range of matching effects is that matching involves 'tagging' stimuli with a match or non-match label, and that retention of this tag across the latency range (for the purpose of response preparation) is yet another sub-process of the N-back task

that's overlaid with replacement and shift, sub-processes whose function is to prepare for processing the next trial in the sequence. Based on patterns in the match effects observed across the two experiments, a further speculation is that the 'match' tag is a verbal operation whereas the 'non-match' tag is a non-verbal (possibly spatial) operation. In the present experiment, in anterior areas, the replacement sub-process was left-lateralized in the verbal and right-lateralized in the spatial task. Match and non-match, respectively, had exactly the same pattern. In posterior areas, the verbal-spatial lateralization was reversed, as was the match vs. non-match pattern. In Experiment 1 as well, left- and right-lateralization of verbal and spatial tasks in the shift sub-process were mirrored by lateralization for match and non-match cases, respectively. Further research is required for a better understanding of matching effects and, more generally, interactions between sub-processes of the N-back task.

Chapter 5. General Discussion

5.1. Overview of experimental results

ERP Data from all the three experiments were analyzed by means of behavioral analysis, general and difference waveforms. Experiment 1 and 2 were conceptual (top-down) whereas Experiment 3 was data-driven (bottom-up). Experiment 3 was the counterpart of Experiment 1 whereas the purpose of Experiment 2 was to test cross-domain interference and justify Experiment 3. Therefore, Experiment 2 was in different line with Experiment 1 and 3.

Table 5-1 shows original ERP results across Experiment 1 and 3 whereas Table 5-2 shows difference ERPs across these two experiments.

		Experiment 1				Experiment 3		
		EPC	P2a	N2	P3	EPC	P2a	N2	P3
Task	L	Spatial>Verbal							
	M	Spatial>Verbal							
Stimulus	L		Match>non-Match	Match>non-Match	Match>non-Match		Match>non-Match	Match>non-Match	Match>non-Match
	M		Match>non-Match	Match>non-Match	Match>non-Match		Match>non-Match	Match>non-Match	Match>non-Match
Stimulus × Task	L		(Match minus non-Match):Spatial>Verbal					(Match minus non-Match): Verbal>Spatial	(Match minus non-Match): Verbal>Spatial
	M			(Match minus non-Match):Verbal>Spatial	(Match minus non-Match):Verbal>Spatial			(Match minus non-Match): Verbal>Spatial	(Match minus non-Match): Verbal>Spatial
Hemisphere	L					L>R in Spatial; L<R in Verbal	L>R in Spatial; L<R in Verbal	L>R in Spatial; L<R in Verbal	
N-Back	L	2>1>0	2>1>0	2>1>0		2>1>0	2>1>0	2>1>0	2>1>0
	M	2>1>0	2>1>0	2>1>0		2>1>0	2>1>0	2>1>0	
N-Back × Task	L								
	M				(Verbal minus Spatial): 0=1>2				
Hemisphere × Stimulus	L								
Hemisphere × Stimulus × Task	L		(Match minus non-Match): L>R in Spatial; L<R in Verbal	(Match minus non-Match): L>R in Spatial; L<R in Verbal	(Match minus non-Match): L>R in Spatial; L<R in Verbal				
Hemisphere × N-Back	L	R>L in 2-Back, others R=L							
Hemisphere × N-Back × Task	L		0:L>R->2:R>L in Spatial; 0:R>L->2:L>R in Verbal						
N-Back × Stimulus	L			(Match minus non-Match) largest in 2-back	Spatial: L>R ; Verbal:R>L ;L-R vertes			(Match minus non-Match): 0=1<2	
	M								
N-Back × Stimulus × Task	L						*		
	M			(Match minus non-Match): 0>2>1 in Spatial; 2>1>0 in Verbal				*	
Hemisphere × N-Back × Stimulus × Task	L								

		Experiment 1				Experiment 3			
		EPC	P2a	N2	P3	EPC	P2a	N2	P3
Task	L	Spatial>Verbal							
	M	Spatial>Verbal							
Stimulus	L		Match>non-Match	Match>non-Match	Match>non-Match		Match>non-Match	Match>non-Match	Match>non-Match
	M		Match>non-Match	Match>non-Match	Match>non-Match		Match>non-Match	Match>non-Match	Match>non-Match
Stimulus × Task	L		(Match minus non-Match):Spatial>Verbal					(Match minus non-Match): Verbal>Spatial	(Match minus non-Match): Verbal>Spatial
	M			(Match minus non-Match):Verbal>Spatial	(Match minus non-Match):Verbal>Spatial			(Match minus non-Match): Verbal>Spatial	(Match minus non-Match): Verbal>Spatial
Hemisphere	L					L>R in Spatial; L<R in Verbal	L>R in Spatial; L<R in Verbal	L>R in Spatial; L<R in Verbal	
N-Back	L	2>1>0	2>1>0	2>1>0		2>1>0	2>1>0	2>1>0	2>1>0
	M	2>1>0	2>1>0	2>1>0		2>1>0	2>1>0	2>1>0	
N-Back × Task	L								
	M				(Verbal minus Spatial): 0=1>2				
Hemisphere × Stimulus	L								
Hemisphere × Stimulus × Task	L		(Match minus non-Match): L>R in Spatial; L<R in Verbal	(Match minus non-Match): L>R in Spatial; L<R in Verbal	(Match minus non-Match): L>R in Spatial; L<R in Verbal				
Hemisphere × N-Back	L	R>L in 2-Back, others R=L							
Hemisphere × N-Back × Task	L		0:L>R->2:R>L in Spatial; 0:R>L->2:L>R in Verbal						
N-Back × Stimulus	L			(Match minus non-Match) largest in 2-back	Spatial: L>R ; Verbal:R>L ;L-R vertes			(Match minus non-Match): 0=1<2	
	M								
N-Back × Stimulus × Task	L						*		
	M			(Match minus non-Match): 0>2>1 in Spatial; 2>1>0 in Verbal				*	
Hemisphere × N-Back × Stimulus × Task	L								

Table 5-1. *Summary of statistically significant effects in the ANOVA of original ERP waveforms. L/M: Lateral/Medial; L/R: Left/Right; 0/1/2: N-back*

Effects	Experiment 1		Experiment 2	
	RT	Accuracy	RT	Accuracy
Behavior				
N-back Task	Increased with N	Decreased with N	Increased with N	Decreased with N
Stimulus		More errors in spatial than in verbal	Spatial > Verbal	
Stimulus×Task	Non-match > match in Spatial; Non-match < match in Verbal	More errors for match than for non-match	Match > Non-match	
Stimulus×N-back	Non-match < match in 0-back; Non-match = match in 1-back; Non-match > match in 2-back		Match > Non-match by more in spatial vs. verbal	
			Match > non-match was greater for higher N	
Latency (ms) / Effects	200-400 / 400-600	600-800	200-400 / 400-600	600-800
Replacement ERP				
AC/P	A<C<P	A<C<P	A>P>C	
AC/P×Task		A<C<P, where under verbal increase steeper		
Stimulus×Task			Spatial: match<non-match; Verbal: match>non-match	
Hemi				L>R
AC/P×Hemi×Task			Anterior: spatial L<R, verbal L>R; Posterior: spatial L>R, verbal R>L	
Stimulus×Hemi		Left: non-Match>Match; Right: none		
Stimulus×Hemi×Task			Match: spatial L>R, verbal L<R; non-Match: spatial L<R, verbal L>R	Match: spatial L>R, verbal L<R; non-Match: none
AC/P×Stimulus×Hemi			Anterior: match L>R, non-match L<R; Posterior: match L<R, non-match L>R	Posterior: match L<R, non-match L>R
Shift ERP				
AC/P	A>C>P	C>A>P		
Stimulus	Match>non-Match	Match>non-Match		
Hemi×Task	Spatial L<R, Verbal L>R			
AC/P×Stimulus×Task	Anterior and Central: Match>non-Match under Verbal; non-Match>Match under Spatial. Posterior: Spatial>Verbal under all.			
Stimulus×Hemi	Match: L>R, non-Match: R>L	Match: L>R, non-Match: R>L		

Table 5-2. *Summary of statistically significant effects in the ANOVA of difference waveforms. A: Anterior; C: Central; P: Posterior; L: Left; R: Right.*

5.2. Data consistency across experiments

Experiment 1 and Experiment3 were designed for different processing. Here Experiment 1 and 3 are compared and their difference and similarity are found out. The brand new theoretical model derived by logical analyses on memorization in n-back tasks is well confirmed by difference waveform analyses across Experiment 1 and 3.

5.2.1. Behavioral data

As expected, RT and error increased with load as n increased. In Experiment 1, non-match RT was generally longer than match RT except in 0-back and 1-back verbal tasks. In Experiment 3, the spatial task took longer to do and the RT difference between matching and non-matching trials was also greater in the spatial task than in the verbal task. Verbal 2-back match-RT was shorter than non-match RT in Experiment 1 whereas verbal 2-back match-RT was longer than non-match RT in Experiment 3. The difference in the 2-back condition was even more pronounced than those in 0-back and 1-back conditions. Error rate in match trials was higher than non-match trials in Experiment 1. In contrast, error rate tended to be lower in match trials than non-match trials in Experiment 3.

In Experiment 1, cross-domain interference did act (Chen, Mitra, & Schlaghecken, 2007),see also Chapter 3) especially in spatial tasks because of Stroop's effect (MacLeod, 1991), which increased the "penetration" of verbal features. In contrast, cross-domain interference was eliminated in Experiment 3. Therefore, Experiment 3 can be viewed as "un-distracted" condition whereas Experiment1 as "interfered" condition. It is reasonable that the cross-domain interference blurred the pattern at decision and caused higher error rate in match trials (all the features should be matched) than in non-match trials (any one feature

unmatched is enough). Something interesting is that RT and error went in opposite trends both in Experiment 1 and 3. It should be noted that RT only reflected correct responses. The opposite trend between RT and error implies that different processes were engaged between correct and error response. (Fernandez *et al.*, 1998) suggests that incorrect responses are predictable, which may cause different strategies in data processing. Obviously, we cannot only explain that longer RT or higher ER as higher difficulty because they were in different direction. However, they are meaningful because they went exactly the opposite trends rather than random.

5.2.2. General ERP waveforms

Match waveforms were more positive-going than non-match ones at P2, N2, and P3 latency windows in both Experiment 1 and 3. In the higher latency, i.e., N2 and P3, difference between match and non-match amplitudes was larger in verbal than in spatial in both Experiment 1 and 3. The non-match amplitude tended to be more negative for the verbal than for the spatial task. Domain-specific lateralization was seen in EPC as well as P2A and N2 latency, but always showing bigger amplitudes in left hemisphere in the spatial task and bigger amplitude in right hemisphere in the verbal task.

The enhancement at post-EPC latency were consistent with the classical findings

from oddball paradigm with target instructions (Chapman & Bragdon, 1964; Donchin & Cohen, 1967; Picton & Hillyard, 1974) and predictions (Suwazono, Machado, & Knight, 2000). The target effects at N2 and P3 might be mainly driven by the verbal non-match negativity, which did show up in Exp1 and appears to be far more pronounced in the Experiment 3. The verbal non-match effect indicates that 'rejecting' a verbal non-match stimulus is a process requiring high-level, frontally mediated inhibitory control. A possible explanation for the reverse of the standard lateralization is that the traditional lateralization effects start only at the late latency (600-1000 ms) of information processing rather than the early one, which has been reported in (Ruchkin *et al.*, 1992).

5.2.3. Difference waveforms

This study presented a logical analysis of the n-back task, and tested the hypothesis that the task has a replacement sub-process of working memory that is primarily data-driven, and a shift sub-process that is primarily conceptually controlled. In a conceptually controlled version of the task (Experiment 1), the stimuli used were identical, and attribute of interest (identity or location) was given by instructions; thus, according to hypothesis, domain-specific lateralization was expected in the shift but not in the replacement sub-process. In a data-driven version of the task

(Experiment 2), the attribute of interest was given by the appearance of stimuli; therefore, domain-specific lateralization was expected in replacement but not in shift. It was hypothesized that the replacement sub-process is related to perceptual processes in the posterior areas whereas the shift sub-process is related to executive processes in the frontal areas. The experimental results broadly supported our logical model that the n-back task consists of three sub-processes: matching, replacement and shift. The data also supported the hypothesis derived from this logical model that the replacement sub-process is primarily data-driven with a posterior locus whereas shift is a more conceptual sub-process with a primarily frontal locus. In addition, the results also indicated that the matching sub-process has electrophysiological effects across the latency range of the subsequent replacement and shift sub-processes. It was suggested that matching may involve an as yet poorly understood tagging process, whereby the match tag is a verbal and the non-match tag is a non-verbal operation.

Overall, the results of the present study suggest that the sub-processes of the n-back task are cortically organized in a rather opportunistic way. When the match criterion was conceptual (Experiment 1), the clear majority of lateralization and match effects were found in the shift sub-process. When the match criterion was perceptual (Experiment 3), these effects were observed in the replacement sub-process. Also, the post-match sub-processes appeared to be lateralized differently based on whether the

stimulus had a match or non-match tag. To the extent that the N-back task is a suitable measure of WM operations, these results suggest that the cortical-temporal organization of the information manipulation sub-processes of WM (i.e., those commonly attributed to a central executive) is heavily dependent upon task domain (verbal or spatial), the manner of definition of task domain (conceptual or perceptual), and the result of the perceptual component of a given trial (i.e., match vs. non-match). A general implication that might be drawn from this is that the n-back task does not involve a unitary and stable information manipulation engine. Rather the manipulation of WM information involves a dynamic functional organization of cortical processes that is assembled on demand, and is structured differently depending upon the current information-processing context. The methodology of detailed logical task analysis, as advocated by (Meegan *et al.*, 2004), and adopted in this study, may have a crucially important role to play in advancing the design and analysis of electrophysiological and imaging studies of the cortical basis of WM operations.

5.3. Conclusion remarks: hints on the neurophysiology of WM

Conventional concepts on memory applies encoding-storage-retrieval model, which is one after another without overlaps. The conventional model with traditional von Neumann's processor, although successful in computer industry, is not likely to stand

for human brain which is parallel processing by fourteen billion neurons and has no central processing unit. Along with the progression of information technology, new non-linear models such as neural networks have been developed and applied in industry. However, the encoding-storage-retrieval model keeps on dominating memory studies as an axiom although no experimental suppoRT can be found to my best knowledge.

Item-recognition tasks follow the standard encoding-storage-retrieval model and are broadly applied in WM tasks. Many advanced models on WM, for example, Baddeley's components, are established on the assumption of computational model and supported well by psychological experiments with item-recognition tasks. In contrast, n-back tasks do not follow the step-by-step convention and tend to execute all the sub-processes at the same time. Because of the holographic nature, n-back tasks were usually analyzed by contrasting the results between different memory loadings (e.g., Ragland *et al.*, 2002; Smith & Jonides, 1997), which hypothesize that tasks with different memory loading consist different components or sub-processes.

Based on (Watter *et al.*, 2001), n-back sub-processes were largely divided into matching and memory, and matching loading is constant whereas memory loading is linear. Therefore, the matching sub-process will be eliminated while calculating difference between results from different memory loading. I further scrutinized the

components of “memory” loading and get the conclusion that 0-back tasks have only one sub-process - matching. 1-back tasks consist of matching and replacement sub-processes whereas 2-back tasks consist of matching, replacement and shift sub-processes. Finally, by simple subtraction, the difference between 1-back and 0-back tasks represents replacement whereas the difference between 2-back and 1-back tasks represents shift.

The logical nature of replacement and shift sub-processes hints more in the topics of perception/manipulation or passive/active processing. Replacement moves information from outer environment (perception, passive processing) into the brain whereas shift moves information within the brain from one location to another (manipulation, active processing). These differences can be shown by experiments with identical stimuli by top-down control (Experiment 1) and with different stimuli by bottom-up control (Experiment 3).

As different aspect of results from similar psychological tasks, behavioral data, general and difference ERP waveforms showed very different patterns. Behavioral data revealed exactly opposite trends between Experiment 1 and 3 whereas general ERP waveforms showed similar patterns in these two experiments. Difference ERP waveforms demonstrated sub-processes of n-back tasks and were most informative. The huge pattern difference between general and difference ERP waveforms hints that

traditional stepwise computational model (encoding-storage-retrieval) may not reflect the holographic WM because its components are concurrent at very short latency. Furthermore, it also suggests the necessity of electrophysiological rather than imaging tools for WM study because complex features can be recorded at the very short latency only by tools with high temporal resolution.

The experimental results from difference waveform analyses support the logical model that the n-back task consists of three sub-processes: matching, replacement and shift and hypothesis derived from this logical model: replacement is data-driven in the posterior area whereas shift is conceptual in the frontal area. The theory correctly predicted patterns in conceptual and data-driven n-back tasks, and is useful for further WM experiments. For example, for a study of the shift impairment in dementia patients, a conceptual rather than data-driven task is recommended (cf. Table 5-2). The similarity between match and task-type in n-back tasks implies theoretical clues and suggests a promising direction for further study.

References

Aguirre, G. K. (2003). Functional imaging in behavioral neurology and neuropsychology. Behavioral Neurology & Neuropsychology. T. E. Feinberg and M. J. Farah. New York, The McGraw-Hill Companies, Inc.: 86.

Aine, C. J., Stephen, J. M., Christner, R., Hudson, D., & Best, E. (2003). Task relevance enhances early transient and late slow-wave activity of distributed cortical sources. *Journal of Computational Neuroscience, 15*, 203-21.

Alekoumbides, A. (1978). Hemispheric dominance for language: quantitative aspects. *Acta Neurologica Scandinavia, 57*, 97-140.

Andres, P., & Van der Linden, M. (2002). Are central executive functions working in patients with focal frontal lesions? *Neuropsychologia, 40*, 835-45.

Anourova, I., Rama, P., Alho, K., Koivusalo, S., Kahnari, J., & Carlson, S. (1999). Selective interference reveals dissociation between auditory memory for location and pitch, *Neuroreport* ,10, 3543-7.

Atkinson, R. C., Shiffrin, R. M. (1971). The control of short-term memory. *Scientific American*, 225, 82-90.

Awh, E., Jonides, J., & Reuter-Lorenz, P. A. (1998). Rehearsal in spatial working memory. *Journal of Experimental Psychology: Human Perception & Performance, 24*, 780-90.

Baddeley, A. D., & Hitch, G. J. (1974). Working memory. In G.A.Bower (Ed.), Recent advances in learning and motivation (Vol. 8, pp. 47–90). New York: Academic Press.

Baddeley, A. D., Thomson, N., & Buchanan, M. (1975). Word lengthand the structure of short-term memory. *Journal of Verbal Learn-ing and Verbal Behavior, 14,* 375–589.

Baddeley, A. D., & Lieberman, K. (1980). Spatial working memory.In R. Nickerson (Ed.), Attention and performance VIII (pp. 521–539). Hillsdale, NJ: Erlbaum.

Baddeley, A. D., Lewis, V. J., & Vallar, G. (1984). Exploring the ar-ticulatory loop. *Quarterly Journal of Experimental Psychology, 36,* 233–52.

Baddeley, A. D., Logie, R., Bressi, S., Della Sala, S., Spinnler, H. (1986). Dementia and working memory. *Quarterly Journal of Experimental Psychology, 38A,* 603-18.

Baddeley, A. D. (1993). Working memory or working attention? In A.D. Baddeley & L. Weiskranta (Eds.), Attention: Selection, awareness, and control. A tribute to Donald Broadbent (pp. 152-170). New York: Oxford University Press.

Baddeley, A. D., & Hitch, G. J. (1994). Developments in the concept of working memory. *Neuropsychology, 8*, 485-93.

Baddeley, A. D., Della Sala, S., Papagno, C., & Spinnler, H. (1997). Dual-task

performance in dysexecutive and nondysexecutive patients with a frontal lesion. *Neuropsychology, 11*, 187-94.

Baddeley, A. D. (2002). Is working memory still working? *European Psychologist, 7*, 85-97.

Bailey, K. R., & Mair, R. G. (2004). Dissociable effects of frontal cortical lesions on measures of visuospatial attention and spatial working memory in the rat. *Cerebral Cortex, 14*, 974-85.

Beauregard, M., Chertkow, H., Bub, D., Murtha, S., Dixon, R., & Evans, A. (1997). The neural substrate for concrete, abstract, and emotional word lexica: A positron emission tomography study. *Journal of Cognitive Neuroscience, 9*, 441-61.

Bennington, J. Y., & Polich, J. (1999). Comparison of P300 from passive and active tasks for auditory and visual stimuli. *International Journal of Psychophysiology, 34*, 171-7.

Berti, S., & Schroeger, E. (2001). A comparison of auditory and visual distraction effects: behavioral and event-related indices. *Cognitive Brain Research, 10*, 265-73.

Bertolino, A., Esposito, G., Callicott, J. H., Mattay, V. S., Van Horn, J. D., Frank, J. A., Berman, K. F., & Weinberger, D. R. (2000). Specific relationship between

prefrontal neuronal n-acetylaspartate and activation of the working memory cortical network in schizophrenia. *American Journal of Psychiatry, 157*, 26-33.

Bish, J. P., Nguyen, V., Ding, L., Ferrante, S., & Simon, T. J. (2004). Thalamic reductions in children with chromosome 22q11.2 deletion syndrome. *Neuroreport, 15*, 1413-5.

Bor, D., Cumming, N., Scott, C. E. L., & Owen, A. M. (2004). Prefrontal cortical involvement in verbal encoding strategies. *European Journal of Neuroscience, 19*, 3365-70.

Brown, G. D. A., & Hulme, C. (1995). Modeling item length effectsin memory span: no rehearsal needed? *Journal of Memory and Language, 34,* 594–621.

Cader, S., Cifelli, A., Abu-Omar, Y., Palace, J., & Matthews, P. M. (2006). Reduced brain functional reserve and altered functional connectivity in patients with multiple sclerosis. *Brain, 129*, 527-37.

Callicott, J. H., Mattay, V. S., Verchinski, B. A., Marenco, S., Egan, M. F., & Weinberger, D. R. (2003). Complexity of prefrontal cortical dysfunction in schizophrenia: more than up or down. *American Journal of Psychiatry, 160*, 2209-15.

Campo, P., Maestu, F., Capilla, A., Fernandez, S., Fernandez, A., & Ortiz, T. (2005). Activity in human medial temporal lobe associated with encoding process in

spatial working memory revealed by magnetoencephalography. *European Journal of Neuroscience, 21*, 1741-8.

Campo, P., Maestu, F., Ortiz, T., Capilla, A., Santiuste, M., Fernandez, A., & Amo, C. (2005). Time modulated prefrontal and parietal activity during the maintenance of integrated information as revealed by magnetoencephalography. *Cerebral Cortex, 15*, 123-30.

Carter, C. S., Perlstein, W., Ganguli, R., Brar, J., Mintun, M., & Cohen, J. D. (1998). Functional hypofrontality and working memory dysfunction in schizophrenia. *American Journal of Psychiatry, 155*, 1285-7.

Casasanto, D. (2003). Hemispheric specialization in prefrontal cortex: effects of verbalizability, imageability and meaning. *Journal of Neurolinguistics, 16*, 361-82.

Chapman, R. M., & Bragdon, H. R. (1964). Evoked responses to numerical and non-numerical visual stimuli while problem solving. *Nature, 203*, 1155-7.

Chein, J. M., & Fiez, J. A. (2001). Dissociation of verbal working memory system components using a delayed serial recall task. *Cerebral Cortex, 11*, 1003-14.

Chen, Y.-N., Mitra S., & Schlaghecken, F. (2007). Interference from the irrelevant domain in N-back tasks: an ERP study. *Acta Neurologica Taiwanica, 16*, 125-35.

Cherry, B. J., Buckwalter, J. G., & Henderson, V. W. (1996). Memory span procedures in Alzheimer's disease. *Neuropsychology, 10*, 286-93.

Clark, L., Iversen, S. D., & Goodwin, G. (2001). A neuropsychological investigation of prefrontal cortex involvement in acute mania. *American Journal of Psychiatry, 158*, 1605-11.

Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature, 386*, 604-8.

Conklin, H. M., Curtis, C. E., Katsanis, J., & Iacono, W. G. (2000). Verbal working memory impairment in schizophrenia patients and their first-degree relatives: evidence from the digit span task. *American Journal of Psychiatry, 157*, 275-7.

Conrad, R., & Hull, A. J. (1964). Information, acoustic confusionand memory span. *British Journal of Psychology*, *55,* 429–37.

Corballis, P. M., Funnell, M. G., & Gazzaniga, M. S. (1999). A dissociation between spatial and identity matching in callosotomy patients. *Neuroreport, 10*, 2183-7.

Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. *Nature, 386*, 608-11.

Cowan, N. (1988). Evolving conceptions of memory storage, selective attention, and

their mutual constraints within the human information-processing system. *Psychological Bulletin, 104*, 163-91.

D'Arcy, R., Ryner, L., Richter, W., Service, E., & Connolly, J. F. (2004). The fan effect in fMRI: left hemisphere specialization in verbal working memory. *Neuroreport, 15*, 1851-5.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*, 9-21.

Deroost, N., & Soetens, E. (2006). Spatial processing and perceptual sequence learning in SRT tasks. *Experimental Psychology, 53*, 16-30.

D'Esposito, M., Detre, J. A., Alsop, D. C., Shin, R. K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature, 378*, 279-81.

D'Esposito, M., Onishi, K., Thompson, H., Robinson, K., Armstrong, C., & Grossman, M. (1996). Working memory impairments in multiple sclerosis: evidence from a dual-task paradigm. *Neuropsychology, 10*, 51-6.

D'Esposito, M., Postle, B. R., Ballard, D., & Lease, J. (1999). Maintenance versus manipulation of information held in working memory: an event-related fMRI study. *Brain and Cognition, 41*, 66-86.

Deutsch, G., Bourbon, W. T., Papanicolaou, A. C., & Eisenberg, H. M. (1988). Visuospatial tasks compared via activation of regional cerebral blood flow. *Neuropsychologia, 26*, 445-52.

Donchin, E., & Cohen, L. (1967). Averaged evoked potentials and intramodality selective attention. *EEG Clinical Neurophysiology, 22*, 537-46.

Eimer, M. (1997). An event-related potential (ERP) study of transient and sustained visual attention to color and form. *Biological Psychology, 44*, 143-60.

Engle RW, Kane MJ, Tuholski SW (1999). Individual differences in working memory capacity and what they tell us about controlled attention, general fluid intelligence and functions of the prefrontal cortex. In Miyake A & SHAH P (Ed.), Models of Working Memory (pp 102-134). Cambridge: Cambridge University Press.

Feigenbaum, J. D., & Morris, R. G. (2004). Allocentric versus egocentric spatial memory after unilateral temporal lobectomy in humans. *Neuropsychology, 18*, 462-72.

Fernandez, T., Harmony, T., Silva, J., Galin, L., Diaz-Comas, L., Bosch, J., Rodriguez, M., Fernandez-Bouzas, A., Y ez, G., Otero, G., & Marosi, E. (1998). Relationship of specific EEG frequencies at specific brain areas with performance. *Neuroreport, 9*, 3680-7.

Fox, P. T., & Raichle, M. E. (1985). Stimulus rate determines regional brain blood flow in striate cortex. *Annals of Neurology, 17,* 303-5.

Fournet, N., Moreaud, O., Roulin, J. L., Naegele, B., & Pellat, J. (2000). Working memory functioning in medicated Parkinson's disease patients and the effect of withdrawal of dopaminergic medication. *Neuropsychology, 14*, 247-53.

Goldman-Rakic, P. S. (2000). Localization of function all over again. *Neuroimage, 11*, 451-7.

Graham, R., & Cabeza, R. (2001). Event-related potentials of recognizing happy and neutral faces. *Neuroreport, 12*, 245-8.

Granholm, E., Morris, S. K., Sarkin, A. J., Asarnow, R. F., & Jeste, D. V. (1997). Pupillary responses index overload of working memory resources in schizophrenia. *Journal of Abnormal Psychology, 106*, 458-67.

Gron, G., Schul, D., Bretschneider, V., Wunderlich, A. P., & Riepe, M. W. (2003). Alike performance during nonverbal episodic learning from diversely imprinted neural networks. *European Journal of Neuroscience, 18*, 3112-20.

Gruber, O. (2001). Effects of domain-specific interference on brain activation associated with verbal working memory task performance. *Cerebral Cortex, 11*, 1047-55.

Hale, S., Myerson, J., Rhee, S. H., Weiss, C. S., & Abrams, R. A. (1996). Selective

interference with the maintenance of location information in working memory. *Neuropsychology, 10*, 228-40.

Halgren, E., Boujon, C., Clarke, J., Wang, C., & Chauvel, P. (2002). Rapid distributed fronto-parieto-occipital processing stages during working memory in humans. *Cerebral Cortex, 12*, 710-28.

Hashimoto, R., Meguro, K., Yamaguchi, S., Ishizaki, J., Ishii, H., Meguro, M., & Sekita, Y. (2004). Executive dysfunction can explain word-list learning disability in very mild Alzheimer's disease: the Tajiri project. *Psychiatry & Clinical Neurosciences, 58*, 54-60.

Henry, J., Petrides, M., St-Laurent, M., & Sziklas, V. (2004). Spatial conditional associative learning: effects of thalamo-hippocampal disconnection in rats. *Neuroreport, 15*, 2427-31.

Herron, J. E., Quayle A. H., Rugg, M. D. (2003). Probability effects on event-related potential correlates of recognition memory. *Cognitive Brain Research, 16,* 66-73.

Hillyard, S. and Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. *Proceedings of the National Academy of Sciences, 95,* 781-787.

Holtzer, R., Stern, Y., & Rakitin, B. C. (2005). Predicting age-related dual-task effects

with individual differences on neuropsychological tests. *Neuropsychology, 19*, 18-27.

Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., & Kennard, C. (2001). Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brain, 124*, 941-52.

Jansen, A., Floel, A., Menke, R., Kanowski, M., & Knecht, S. (2005). Dominance for language and spatial processing: limited capacity of a single hemisphere. *Neuroreport, 16*, 1017-21.

Jensen, O., & Tesche, C. D. (2002). Frontal theta activity in humans increases with memory load in a working memory task. *European Journal of Neuroscience, 15*, 1395-9.

Johnson, B. W., McKenzie, K. J., & Hamm, J. P. (2002). Cerebral asymmetry for mental rotation: effects of response hand, handedness and gender. *Neuroreport, 13*, 1929-32.

Kaiser, J., Walker, F., Leiberg, S., & Lutzenberger, W. (2005). Cortical oscillatory activity during spatial echoic memory. *European Journal of Neuroscience, 21*, 587-90.

Katayama, J., & Polich, J. (1999). Auditory and visual P300 topography from a three-stimulus paradigm. *Clinical Neurophysiology, 110*, 463-8.

Kessels, R., Postma, A., Kappelle, L. J., & de Haan, E. (2000). Spatial memory impairment in patients after tumour resection: evidence for a double dissociation. *Journal of Neurology, Neurosurgery & Psychiatry, 69*, 389-91.

Kessels, R., Postma, A., Wijnalda, E. M., & De Haan, E. (2000). Frontal-lobe Involvement in spatial memory: evidence from PET, fMRI, and lesion studies. *Neuropsychology Review, 10*, 101-13.

Kessler, K., & Kiefer, M. (2005). Disturbing visual working memory: electrophysiological evidence for a role of the prefrontal cortex in recovery from interference. *Cerebral Cortex, 15*, 1075-87.

Kim, J.-J., Kwon, J. S., Park, H. J., Youn, T., Kang, D. H., Kim, M. S., Lee, D. S., & Lee, M. C. (2003). Functional disconnection between the prefrontal and parietal cortices during working memory processing in schizophrenia. *American Journal of Psychiatry, 160*, 919-23.

Klauer, K. C., & Zhao, Z. (2004). Double dissociations in visual and spatial short-term memory. *Journal of Experimental Psychology: General, 133*, 355-81.

Lange, E. B. (2005). Disruption of attention by irrelevant stimuli in serial recall. *Journal of Memory and Language, 53*, 513-31.

Lavric, A., Rippon, G., & Gray, J. R. (2003). Threat-evoked anxiety disrupts spatial

working memory performance: an attentional account. *Cognitive Therapy & Research, 27*, 489-504.

Lawrence, B. M., Myerson, J., & Abrams, R. A. (2004). Interference with spatial working memory: An eye movement is more than a shift of attention. *Psychonomic Bulletin and Review, 11*, 488-94.

Lengenfelder, J., Chiaravalloti, N. D., Ricker, J. H., & DeLuca, J. (2003). Deciphering components of impaired working memory in multiple sclerosis. *Cognitive & Behavioral Neurology, 16*, 28-39.

Leung, H. C., Gore, J. C., & Goldman-Rakic, P. S. (2005). Differential anterior prefrontal activation during the recognition stage of a spatial working memory task. *Cerebral Cortex, 15*, 1742-9.

Li, X., Wong, D., Gandour, J., Dzemidzic, M., Tong, Y., Talavage, T., & Lowe, M. (2004). Neural network for encoding immediate memory in phonological processing. *Neuroreport, 15*, 2459-62.

Logie, R. H., Zucco, G. M., & Baddeley, A. D. (1990). Interference with visual short-term memory. *Acta Psychologica, 75*, 55-74.

Long, J. M., & Kesner, R. P. (1998). Effects of hippocampal and parietal cortex lesions on memory for egocentric distance and spatial location information in rats. *Behavioral Neuroscience, 112*, 480-95.

Ma, Y.-Y., Tian, B. P., & Wilson, F. (2003). Dissociation of egocentric and allocentric spatial processing in prefrontal cortex. *Neuroreport, 14*, 1737-41.

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: an integrative review. *Psychological Bulletin, 109*, 163-203.

Malafouris, L. (2005). The cognitive basis of material engagement:where brain, body and culture conflate. In E. DeMarrais, C. Gosden & C. Renfrew (Eds.), *Rethinking Materiality, the Engagement of Mind with the Material World*. Cambridge: McDonald Institute.

Malhotra, P., Jager, H. R., Parton, A., Greenwood, R., Playford, E. D., Brown, M. M., Driver, J., & Husain, M. (2005). Spatial working memory capacity in unilateral neglect. *Brain, 128*, 424-35.

McElree, B. (2001). Working memory and focal attention. *Journal of Experimental Psychology: Learning, Memory, & Cognition, 27*, 817-35.

McEvoy, L. K., Smith, M. E., & Gevins, A. (1998). Dynamic cortical networks of verbal and spatial wordking memory: Effects of memory load and task practice. *Cerebral Cortex, 8*, 563-74.

McFie, J., Piercy, M. F., & Zangwill, O. L. (1950). Visual-spatial agnosia associated with lesions of the right cerebral hemisphere. *Brain: a Journal of Neurology, 73*, 167-90.

Meegan, D. V., & Honsberger, M. J. M. (2005). Spatial information is processed even when it is task-irrelevant: Implications for neuroimaging task design. *Neuroimage, 25*, 1043-55.

Meegan, D. V., Purc-Stephenson, R., Honsberger, M. J. M., & Topan, M. (2004). Task analysis complements neuroimaging: an example from working memory research. *Neuroimage, 21*, 1026-36.

Mendrek, A., Kiehl, K. A., Smith, A. M., Irwin, D., Forster, B. B., & Liddle, P. F. (2005). Dysfunction of a distributed neural circuitry in schizophrenia patients during a working-memory performance. *Psychological Medicine, 35*, 187-96.

Miyake, A., Friedman, N. P., Rettinger, D. A., Shah, P., & Hegarty, M. (2001). How are visuospatial working memory, executive functioning, and spatial abilities related? a latent-variable analysis. *Journal of Experimental Psychology: General, 130*, 621-40.

Miyake, A., & Shah, P. (1999). Mechanisms of active maintenance and executive control. In *Models of working memory*: New York, NY: Cambridge University Press.

Morey, C. C., & Cowan, N. (2005). When do visual and verbal memories conflict? the importance of working-memory load and retrieval. *Journal of Experimental Psychology: Learning, Memory, & Cognition, 31*, 703-13.

Morris, R. G. (1994). Working memory in Alzheimer-type dementia. *Neuropsychology, 8*, 544-54.

Mottaghy, F. M., Doring, T., Muller-Gartner, H.-W., Topper, R., & Krause, B. J. (2002). Bilateral parieto-frontal network for verbal working memory: an interference approach using repetitive transcranial magnetic stimulation (rTMS). *European Journal of Neuroscience, 16*, 1627-32.

Muller, M. M., & Hillyard, S. (2000). Concurrent recording of steady-state and transient event-related potentials as indices of visual-spatial selective attention. *Clinical Neurophysiology, 111*, 1544-52.

Muller, R.-A., Rothermel, R. D., Behen, M. E., Muzik, O., Mangner, T. J., & Chugani, H. T. (1997). Receptive and expressive language activations for sentences: a PET study. *Neuroreport, 8*, 3767-70.

Murray, D. J. (1968). Articulation and acoustic confusability inshort-term memory. *Journal of Experimental Psychology, 78*,679–684.

Neath, L, & Nairne, J.S. (1995). Word-length effects in immediatememory: Overwriting trace-decay theory. *Psychonomic Bulletinand Review, 2,* 429–441.

Nelson, C. A., Monk, C. S., Lin, J., Carver, L. J., Thomas, K. M., & Truwit, C. L. (2000). Functional neuroanatomy of spatial working memory in children. *Developmental Psychology, 36*, 109-16.

Nobre, A. C. (2001). Orienting attention to instants in time. *Neuropsychologia, 39*, 1317-28.

Oberauer, K. (2001). Removing irrelevant information from working memory: a cognitive aging study with the modified Sternberg task. *Journal of Experimental Psychology: Learning, Memory, & Cognition, 27*, 948-57.

Oliveri, M., Turriziani, P., Carlesimo, G. A., Koch, G., Tomaiuolo, F., Panella, M., & Caltagirone, C. (2001). Parieto-frontal interactions in visual-object and visual-spatial working memory: evidence from transcranial magnetic stimulation. *Cerebral Cortex, 11*, 606-18.

Olivers, C. N. L. (2004). Blink and shrink: the effect of the attentional blink on spatial processing. *Journal of Experimental Psychology: Human Perception & Performance, 30*, 613-31.

O'Reilly, R. C., Braver, T. S., & Cohen, J. D. (1997). A biologically-based computational model of working memory. In A. Miyake & P. Shah (Eds.), *Models of Working Memory: Mechanisms of Active Maintenance and Executive Control*. New York: Cambridge University Press.

Ota, H., Fujii, T., Tabuchi, M., Sato, K., Saito, J., & Yamadori, A. (2003). Different spatial processing for stimulus-centered and body-centered representations. *Neurology, 60*, 1846-8.

Owen, A., Stern, S., Look, R., Tracey, I., Rosen, B., & Petrides, M. (1998). Functional organization of spatial and nonspatial working memory processing within the human lateral frontal cortex. *Proceedings of the National Academy of Sciences, 95*.

Papanicolaou, A. C., Levin, H. S., & Eisenberg, H. M. (1984). Evoked potential correlates of recovery from aphasia after focal left hemisphere injury in adults. *Neurosurgery, 14*, 412-5.

Parasuraman, R., & Haxby, J. V. (1993). Attention and brain function in Alzheimer's disease: a review. *Neuropsychology, 7*, 242-72.

Paulesu, E., Frith, C. D., & Frackowiak, R. S. J. (1993). The neural correlates of the verbal component of working memory. *Nature, 362*, 342-5.

Perlstein, W. M., Carter, C. S., Noll, D. C., & Cohen, J. D. (2001). Relation of prefrontal cortex dysfunction to working memory and aymptoms in schizophrenia. *American Journal of Psychiatry, 158*, 1105-13.

Petersen, S. E., Fox, P. T., Snyder, A. Z., & Raichle, M. E. (1990). Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. *Science, 249*, 1041-4.

Petrides, M. (1994). The frontal lobes and behaviour. *Current Opinion in Neurobiology, 4*.

Picton, T. W., & Hillyard, S. A. (1974). Human auditory evoked potentials. II: Effects of attention. *Clinical Neurophysiology, 36*, 191-9.

Pierrot-Deseilligny, C. H., Muri, R. M., Nyffeler, T., & Milea, D. (2005). The role of the human dorsolateral prefrontal cortex in ocular motor behavior. *Annals of the New York Academy of Sciences*, 239-51.

Pourtois, G., Vandermeeren, Y., Olivier, E., & de Gelder, B. (2001). Event-related TMS over the right posterior parietal cortex induces ipsilateral visuo-spatial interference. *Neuroreport, 12*, 2369-74.

Ragland, J. D., Turetsky, B. I., Gur, R. C., Gunning-Dixon, F., Turner, T., Schroeder, L., Chan, R., & Gur, R. E. (2002). Working memory for complex figures: an fMRI comparison of letter and fractal n-back tasks. *Neuropsychology, 16*, 370-9.

Ravizza, S. M., Behrmann, M., & Fiez, J. A. (2005). Right parietal contributions to verbal working memory: Spatial or executive? *Neuropsychologia, 43*, 2057-67.

Riegler, A. (2005). Constructive memory. *Kybernetes, 34*, 89-104.

Roberts, R., & Gibson, E. (2002). Individual differences in sentence memory. *Journal of Psycholinguistic Research, 31*, 573-98.

Robertson, E. M., Tormos, J. M., Maeda, F., & Pascual-Leone, A. (2001). The role of the dorsolateral prefrontal cortex during sequence learning is specific for spatial

information. *Cerebral Cortex, 11*, 628-35.

Rombouts, S. A., van Swieten, J. C., Pijnenburg, Y. A. L., Goekoop, R., Barkhof, F., & Scheltens, P. (2003). Loss of frontal fMRI activation in early frontotemporal dementia compared to early AD. *Neurology, 60*, 1904-8.

Ross, P., & Segalowitz, S. J. (2000). An EEG coherence test of the frontal dorsal versus ventral hypothesis in n-back working memory. *Brain and Cognition, 43*, 375-9.

Ruchkin, D. S., Johnson, J., Ray, Grafman, J., Canoune, H., & Ritter, W. (1992). Distinctions and similarities among working memory processes: an event-related potential study. *Cognitive Brain Research, 1*, 53-66.

Rueda, M. R., Posner, M. I., Rothbart, M. K., & Davis-Stober, C. P. (2004). Development of the time course for processing conflict: An event-related potentials study with 4 year olds and adults. *BMC Neuroscience, 5*, 39.

Sakai, K., & Passingham, R. E. (2004). Prefrontal selection and medial temporal lobe reactivation in retrieval of short-term verbal information. *Cerebral Cortex, 14*, 914-21.

Schatz, J., Craft, S., Koby, M., & DeBaun, M. R. (2004). Asymmetries in visual-spatial processing following childhood stroke. *Neuropsychology, 18*, 340-52.

Schendan, H. E., Ganis, G., & Kutas, M. (1998). Neurophysiological evidence for visual perceptual categorization of words and faces within 150 ms. *Psychophysiology, 35*, 240-51.

Scott, S. K., Holmes, A., Friston, K. J., & Wise, R. J. S. (2000). A thalamo-prefrontal system for representation in executive response choice. *Neuroreport, 11*, 1523-7.

Sciffrin RM, Schneider W (1977). Controlled and automatic human information processing: II. Perceptual learning, automatic attending, and a general theory. *Psychological Review, 84,* 127-190.

Siok, W. T., Perfetti, C. A., Jin, Z., & Tan, L. H. (2004). Biological abnormality of impaired reading is constrained by culture. *Nature, 431*, 71-6.

Smith, E. E., & Jonides, J. (1997). Working memory: a view from neuroimaging. *Cognitive Psychology, 33*, 5-42.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*, 1657-61.

Stephan, K. E., Marshall, J. C., Friston, K. J., Rowe, J. B., Ritzl, A., Zilles, K., & Fink, G. R. (2003). Lateralized cognitive processes and lateralized task control in the human brain. *Science, 301*, 384-6.

Sternberg, S. (1966). High-speed scanning in human memory. *Science, 153*, 652-4.

Stevens, A. A., Goldman-Rakic, P. S., Gore, J. C., Fulbright, R. K., & Wexler, B. E. (1998). Cortical dysfunction in schizophrenia during auditory word and tone working memory demonstrated by functional magnetic resonance imaging. *Archives of General Psychiatry, 55*, 1097-103.

Stins, J. F., de Sonneville, L. M. J., Groot, A. S., Polderman, T. C., van Baal, C. G., & Boomsma, D. I. (2005). Heritability of selective attention and working memory in preschoolers. *Behavior Genetics, 35*, 407-16.

Stowe, L. A., Broere, C. A. J., Paans, A. M. J., Wijers, A. A., Mulder, G., Vaalburg, W., & ZwaRT, F. (1998). Localizing components of a complex task: sentence processing and working memory. *Neuroreport, 9*, 2995-9.

Suwazono, S., Machado, L., & Knight, R. T. (2000). Predictive value of novel stimuli modifies visual event-related potentials and behavior. *Clinical Neurophysiology, 111*, 29-39.

Tan, H.-Y., Choo, W.-C., Fones, C. S. L., & Chee, M. W. L. (2005). fMRI study of maintenance and manipulation processes within working memory in first-episode schizophrenia. *American Journal of Psychiatry, 162*, 1849-58.

Ullsperger, P., Metz, A., & Gille, H. (1988). The P300 component of the event-related brain potential and mental effort. *Ergonomics, 31*, 1127-37.

Vecchi, T., Saveriano, V., & Paciaroni, L. (1998). Storage and processing working

memory functions in Alzheimer-type dementia. *Behavior Neurology, 11*, 227-31.

Veltman, J. C., Brouwer, W. H., van Zomeren, A. H., & van Wolffelaar, P. C. (1996). Central executive aspects of attention in subacute severe and very severe closed head injury patients: planning, inhibition, flexibility, and divided attention. *Neuropsychology, 10*, 357-67.

Wang, Y., Tang, X., Kong, J., Zhuang, D., & Li, S. (1998). Different systems in human brain are involved in presemantic discrimination of pictures as revealed by event-related potentials. *Neuroscience Letters, 257*, 143-6.

Watter, S., Geffen, G. M., & Geffen, L. B. (2001). The n-back as a dual-task: P300 morphology under divided attention. *Psychophysiology, 38*, 998-1003.

Wilson, F., Scalaidhe, S., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science, 260*, 1955-8.

Wolach, I., & Pratt, H. (2001). The mode of short-term memory encoding as indicated by event-related potentials in a memory scanning task with distractions. *Clinical Neurophysiology, 112*, 186-97.

Wolber, M., & Wascher, E. (2005). The posterior contralateral negativity as a temporal indicator of visuo-spatial processing. *Journal of Psychophysiology, 19*, 182-94.

Appendix

Appendix 1. Test-words used in the N-back tasks.

Negative	Neutral	Positive
doom	zone	calm
ugly	lens	joke
curse	scan	cheer
upset	zero	medal
grave	lawn	laugh
abuse	wrist	eager
solemn	onion	amazed
punish	slope	tender
doubts	deduct	ardent
misery	recruit	lively
stupid	sooner	warmth
ashamed	mention	hopeful
penalty	library	excited
avoided	acquaint	pleased
suicide	barbecue	carefree
despair	conclude	faithful
poverty	fragment	glorious
hopeless	aluminum	enjoying
helpless	retained	vitality
rejected	indirect	relieved

Appendix 2. Instructions before a block.

BLOCK A: LOCATION, 0-BACK
In this block, every time you see a word, you should press the YES button if the word occurred in the same screen LOCATION as the VERY FIRST WORD OF THE BLOCK.

BLOCK B: LOCATION, 1-BACK
In this block, every time you see a word, you should press the YES button if the word occurred in the SAME SCREEN LOCATION as the WORD IN THE PREVIOUS TRIAL.

BLOCK C: LOCATION, 2-BACK
In this block, every time you see a word, you should press the YES button if the word occurred in the SAME SCREEN LOCATION as the WORD IN THE TRIAL BEFORE THE PREVIOUS TRIAL.

BLOCK D: WORD, 0-BACK
In this block, every time you see a word, you should press the YES button if the WORD is the same as the VERY FIRST WORD OF THE BLOCK.

BLOCK E: WORD, 1-BACK
In this block, every time you see a word, you should press the YES button if the WORD is the same as the WORD IN THE PREVIOUS TRIAL.

BLOCK F: WORD, 2-BACK
In this block, every time you see a word, you should press the YES button if the WORD is the same as the WORD IN THE TRIAL BEFORE THE PREVIOUS TRIAL.

Appendix 3. Source code of the program for testing a block.

```
#include <conio.h>
#include <dir.h>
#include <dos.h>
#include <graphics.h>
#include <math.h>
#include <stdio.h>
#include <stdlib.h>
#include <string.h>
#include <time.h>

char sequences[3][10][65],word_sets[3][20][10];

char argv[10][10];
int argc;

int
wordxy[8][2]={{30,10},{35,10},{40,10},{30,11},{40,11},{30,12},{35,12},{40,12}};

int
trials[64],itrials[64],response_keys[64],reaction_times[64],stimuli[64],corrects[64],ist
imuli[64],icorrects[64];

void makesequence(void)
{
 int i,j,count;
 char target[64];

 randomize();
 // 0-back

 for(i=0;i<10;i++)
 {
  //randomize();
  sequences[0][i][0]=random(8)+49;
  count=0;
```

```
  while(count<32)
  {
   count=0;
   for(j=1;j<64;j++)
   {
    target[j]=random(2);
    if(j>=3)
    {
     if(target[j]*target[j-1]*target[j-2]==1) target[j]=0; //avoid more than 3 targets
together
    }
    if(target[j]==1) count++;
    if(count>=32) break;
   }
  }
  for(j=1;j<64;j++)
  {
   if(target[j]==1) sequences[0][i][j]=sequences[0][i][0];
   else
   {
      do sequences[0][i][j]=random(8)+49;
      while(sequences[0][i][j]==sequences[0][i][0]);
   }
  }
  sequences[0][i][64]=0;
  printf("%s\n",sequences[0][i]);

  //printf(" ");
  //for(j=1;j<64;j++) printf("%d",target[j]);
  //printf("\n");
 }

 // 1-back

 for(i=0;i<10;i++)
 {
  //randomize();
  sequences[1][i][0]=random(8)+49;
```

```
   count=0;
   while(count<32)
   {
    count=0;
    for(j=1;j<64;j++)
    {
     target[j]=random(2);
     if(j>=3)
     {
      if(target[j]*target[j-1]*target[j-2]==1) target[j]=0; //avoid more than 4 targets
together
     }
     if(target[j]==1) count++;
     if(count>=32) break;
    }
   }
   for(j=1;j<64;j++)
   {
    if(target[j]==1) sequences[1][i][j]=sequences[1][i][j-1];
    else
    {
       do sequences[1][i][j]=random(8)+49;
       while(sequences[1][i][j]==sequences[1][i][j-1]);
    }
   }
   sequences[1][i][64]=0;
   printf("%s\n",sequences[1][i]);

   //printf(" ");
   //for(j=1;j<64;j++) printf("%d",target[j]);
   //printf("\n");
  }

 // 2-back

 for(i=0;i<10;i++)
 {
```

```
    //randomize();
    sequences[2][i][0]=random(8)+49;
    sequences[2][i][1]=random(8)+49;

    count=0;
    while(count<32)
    {
      count=0;
      for(j=2;j<64;j++)
      {
        target[j]=random(2);
        if(j>=4)
        {
          if(target[j]*target[j-1]*target[j-2]==1) target[j]=0; //avoid more than 3 targets
together
        }
        if(target[j]==1) count++;
        if(count>=32) break;
      }
    }

    for(j=2;j<64;j++)
    {
      if(target[j]==1) sequences[2][i][j]=sequences[2][i][j-2];
      else
      {
        do sequences[2][i][j]=random(8)+49;
        while(sequences[2][i][j]==sequences[2][i][j-2]);
      }
    }
    sequences[2][i][64]=0;
    printf("%s\n",sequences[2][i]);

    //printf("     ");
    //for(j=2;j<64;j++) printf("%d",target[j]);
    //printf("\n");
  }
}
```

```
void loaddata(void)
{
 FILE *rp;
 int i,j;

 // load sequences
 makesequence();

 // load word_sets
 if((rp=fopen("words.nbk","r"))==NULL)
 {
  printf("Error!\7\n");
  exit(255);
 }
 for(i=0;i<3;i++)
 {
  for(j=0;j<20;j++) fgets(word_sets[i][j],255,rp);
 }
 fclose(rp);
}

// n=N-back
// word_set 0=negative 1=neutral 2=positive
void block(int n,int word_set,int verbal_spatial,int number_of_trials,int feedback,int
right_key)
{
 int i,j,k,x,y,elapse_time1,elapse_time2,target_signal;
 char test_words[8][10];
 unsigned long int start_time,present_time;

 _setcursortype(_NOCURSOR);
 elapse_time1=CLK_TCK*500/1000;
 elapse_time2=CLK_TCK*1500/1000+elapse_time1;

 if(feedback==0)
 {
  outportb(888,254);
```

```
  delay(1);
  outportb(888,0);
}

// select 8 from 20 word_sets
randomize();
x=random(20);
for(i=0;i<8;i++)    strcpy(test_words[i],word_sets[word_set][(i+x)%20]);

corrects[0]=corrects[1]=icorrects[0]=icorrects[1]=1;

// choose sequencesuence
randomize();
x=random(10);
randomize();
y=random(10);
for(i=0;i<number_of_trials;i++)
{
  target_signal=0;
  trials[i]=j=sequences[n][x][i]-49;
  itrials[i]=k=sequences[n][y][i]-49;
  reaction_times[i]=response_keys[i]=0;

  // fixation cross
  clrscr();
  gotoxy(37,11);
  printf("X");
  delay(350);

  //cross disappears
  clrscr();
  delay(350);

  // target signal?
  switch(n)
  {
    case 0:
      if(i<1) break;
```

```
   if(trials[i]==trials[0]) target_signal=1;
   else target_signal=0;
  break;

  case 1:
   if(i<1) break;
   if(trials[i]==trials[i-1]) target_signal=1;
   else target_signal=0;
  break;

  case 2:
   if(i<2) break;
   if(trials[i]==trials[i-2]) target_signal=1;
   else target_signal=0;
  break;
}

// irrelevant target signal?
switch(n)
{
  case 0:
   if(i<1) break;
   if(itrials[i]==itrials[0]) istimuli[i]=1;
   else istimuli[i]=0;
  break;

  case 1:
   if(i<1) break;
   if(itrials[i]==itrials[i-1]) istimuli[i]=1;
   else istimuli[i]=0;
  break;

  case 2:
   if(i<2) break;
   if(itrials[i]==itrials[i-2]) istimuli[i]=1;
   else istimuli[i]=0;
  break;
}
```

```
// ****trigger signal send here****
if(target_signal)
{
 stimuli[i]=1;
 outportb(888,1);
 delay(2);
 outportb(888,0);
}
else
{
 stimuli[i]=0;
 outportb(888,2);
 delay(2);
 outportb(888,0);
}

// word appear on screen
if(verbal_spatial)
{
 gotoxy(wordxy[j][0],wordxy[j][1]); //spatial--let word_sets random
 printf("%s",test_words[k]);
}
else
{
   gotoxy(wordxy[k][0],wordxy[k][1]); // verbal--let position random
   printf("%s",test_words[j]);
}

start_time=clock();
do
{
 present_time=clock()-start_time;
 if(kbhit())
 {
  response_keys[i]=getch();
  reaction_times[i]=present_time*1000/CLK_TCK;
 }
```

```
    }
    while(present_time<elapse_time1);

     // blank screen
    clrscr();
    do
    {
     present_time=clock()-start_time;
     if(kbhit())
     {
      response_keys[i]=getch();
      reaction_times[i]=present_time*1000/CLK_TCK;
     }
    }
    while(present_time<elapse_time2);

    //judgement
    if(response_keys[i]==0)    corrects[i]=icorrects[i]=0;
    else
    {
     switch(n)
     {
      case 0:
       if(i<1) break;

if((response_keys[i]==right_key&&trials[i]==trials[0])||(response_keys[i]!=right_key
&&trials[i]!=trials[0])) corrects[i]=1;
       else corrects[i]=0;

if((response_keys[i]==right_key&&itrials[i]==itrials[0])||(response_keys[i]!=right_ke
y&&itrials[i]!=itrials[0])) icorrects[i]=1;
       else icorrects[i]=0;
      break;

      case 1:
       if(i<1) break;

if((response_keys[i]==right_key&&trials[i]==trials[i-1])||(response_keys[i]!=right_ke
```

```
y&&trials[i]!=trials[i-1])) corrects[i]=1;
        else corrects[i]=0;

if((response_keys[i]==right_key&&itrials[i]==itrials[i-1])||(response_keys[i]!=right_k
ey&&itrials[i]!=itrials[i-1])) icorrects[i]=1;
        else icorrects[i]=0;
       break;

       case 2:
        if(i<2) break;

if((response_keys[i]==right_key&&trials[i]==trials[i-2])||(response_keys[i]!=right_ke
y&&trials[i]!=trials[i-2])) corrects[i]=1;
        else corrects[i]=0;

if((response_keys[i]==right_key&&itrials[i]==itrials[i-2])||(response_keys[i]!=right_k
ey&&itrials[i]!=itrials[i-2])) icorrects[i]=1;
        else icorrects[i]=0;
       break;
     }
   }
   if(feedback)
   {
     gotoxy(35,11);
     if(corrects[i]) printf("CORRECT");
     else printf("WRONG");
     delay(500);
   }
 }
 outportb(888,255);
 delay(1);
 outportb(888,0);
 printf("\7");
   _setcursortype(_NORMALCURSOR);
}

void export(char *fname,int n,int word_set,int task_type,int number_of_trials,int
response_key)
```

```
{
 FILE *wp;
 int i;

 if((wp=fopen(fname,"w"))==NULL)
 {
  printf("Write open Error!\7\n");
  exit(255);
 }


fprintf(wp,"Parameters:%d-back\tword_set=%d\ttask_type=%d\tresponse_key=%c\n\
n",n,word_set,task_type,response_key);
 fprintf(wp,"Trials\tiTrials\tKey\tTime\tStimuli\tCorrect\tiStimuli\tiCorrect\n");
 for(i=0;i<number_of_trials;i++)
 {

fprintf(wp,"%d\t%d\t%d\t%d\t%d\t%d\t%d\t%d\n",trials[i],itrials[i],response_keys[i],
reaction_times[i],stimuli[i],corrects[i],istimuli[i],icorrects[i]);
 }
 fclose(wp);
}

void main(int argc, char **argv)
{
 int n,word_set,task_type,number_of_trials,feedback,response_key;

 if(argc<8)
 {
  printf("\nBLOCK n word_set task_type trials feedback response_key
result_file\n\n");
  printf("n\t\tN-back\nword_set\t0:negative 1:neutral 2:positive\ntask_type\t0:verbal
1:spatial\ntrials\t\tnumber of trials\n");
  printf("feedback\t0:no feedback 1:with feedback\nresponse_key\tthe key for right
response\nresult_file\tfilename for result\n\n");
  printf("N-Back Verbal and Spatial Tasks with Emotional words 1.0\n");
  printf("Copyright 2004 by Yung-Nien Chen, M.D.\n");
  printf("Department of Psychology, University of Warwick, Coventry, UK\n");
```

```
  exit(255);
 }

 loaddata();

 n=atoi(argv[1]);
 word_set=atoi(argv[2]);
 task_type=atoi(argv[3]);
 number_of_trials=atoi(argv[4]);
 feedback=atoi(argv[5]);
 response_key=argv[6][0];

 block(n,word_set,task_type,number_of_trials,feedback,response_key);
 export(argv[7],n,word_set,task_type,number_of_trials,response_key);
}
```